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"TWO CENTURIES OF SERVICE—WHAT OF THE NEXT?"*

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BOSTON

SINCE the Pennsylvania Hospital was founded two hundred years ago, there has probably not been a time when the hospitals and the medical profession of this country faced greater opportunities for public service than they do today. Medicine has more to offer now than it has ever had, not only in healing the sick and injured but also in preventing disease and disability and in restoring the handicapped to usefulness. The public has more confidence in the benefits of medicine than it has ever had, and therefore is more interested than ever in having these benefits.

This situation indeed puts great opportunities before us, but it also brings great problems. How can the best in modern medicine become available to our entire population at a cost we can afford? How, at the same time, can our high professional standards be maintained and advanced? These are the crucial issues we face, and the way in which they are settled will determine the role that our splendid hospitals and our magnificent medical profession will play in the future. Here, too, is a "great debate"; here, too, lie fundamental issues of policy that inevitably must be decided and that call for the highest and most dispassionate kind of professional and public statesmanship.

It is a great honor and privilege to have been called upon to participate in your celebration of the anniversary of one of the most important events in American medical history — the founding of the nation's first hospital, a hospital that has proved to be the ever vital parent-root of teaching hospitals in this country. As a representative of your early daughter, the Massachusetts General Hospital, I bring you sincerest greetings on your birthday and filial good wishes for your next two centuries — at least!

It is peculiarly appropriate that these two hospitals should share, in some part, in this celebration, for they have a history of close relations that goes back nearly one hundred and fifty years. Indeed, it existed, in a way, before either hospital was founded. After all, one of your principal founders, Benjamin Franklin, did come from Boston. We like to think that if he had stayed home, instead of yielding to the charms of Philadelphia, we might have had the first hospital.

The New York Hospital and our hospital in Boston were built on the principles first enunciated in the founding of the Pennsylvania Hospital — and from these same principles sprang the whole proud tradition of the voluntary teaching hospital in America.

The Massachusetts General Hospital, as a matter of fact, owes its very existence to the Pennsylvania Hospital. In the early years of the nineteenth century students of medicine in Boston, having no hospital in which to study clinical material, flocked to Philadelphia to complete their training. Thus, many of the men who were to become prominent in Boston medicine at about the time of the founding of the Massachusetts General Hospital, like George Shattuck, Jacob Bigelow, Walter Channing and George Hayward, came here to study with such distinguished mentors as Benjamin Rush, Caspar Wistar, Philip Syng Physick, John Redman Coxe and Benjamin Barton.

Although the good citizens of Boston appreciated the learning that their young medical men received in Philadelphia, they also were stimulated by it to think that they too needed a general hospital, not only to care for the sick but also to serve as a center of medical education. Thus, a public letter written by Drs. James Jackson and John Collins Warren in 1810, soliciting support for the hospital-to-be in Boston, states: "The means of medical education in New England are.... totally inadequate .... The only medical school of eminence in this country is that at Philadelphia.... A hospital is an institution absolutely essential to a medical school...."

Later, when plans were being drawn by Bulfinch for the Massachusetts General Hospital, the trustees sent him here to study the Pennsylvania Hospital as his model. The compliment was returned a few years later, when the illustrious Kirkbride, planning your Department for Mental and Nervous Diseases, journeyed to Boston to study the McLean

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Hospital, which, as you know, is the hospital for mental disorders associated with the Massachusetts General Hospital.

Such were the beginnings of more than a century of close professional association between the two institutions, the latest example of which was the founding ten years ago of the Hall-Mercer Hospital (also for psychiatry), with a branch at Massachusetts General and another here. It seems very natural, then, for someone from your Boston offshoot to join you today in recognizing Pennsylvania Hospital's outstanding record of accomplishment during two hundred years.

And it is indeed a record to be proud of. Pennsylvania Hospital is in its distinguished position today not only because it was our first hospital but also because it has continued to be a leader throughout its career. Here, as you know, clinical teaching was initiated in this country. The hospital was at first simply a place where apprentice physicians could walk the wards, but it soon became a principal focus of systematic training for the students of what is now the University of Pennsylvania Medical School, to which, of course, were later added students from the Woman's Medical College and from Jefferson Medical College.

Here, too, were established the first out-patient department (even before the founding of the Philadelphia Dispensary), one of the earliest medical libraries in this country and the first clinical amphitheatre (later to be the model for the amphitheatre at Massachusetts General Hospital). In medical science, physicians at Pennsylvania Hospital long ago led in describing hemophilia and in performing the first planned operation for appendicitis. More recently they have been leaders in many other fields, such as caudal analgesia, the first successful drying of human blood plasma, important studies on insulin, electric shock and carbon-dioxide treatment in mental illness, electrophysiology of nerve, nutrition in pregnancy, hematology and the clinical testing of neomycin, to mention but a few.

You have also pioneered in the field of preventive medicine, especially in making available to the whole community, rich or poor alike, the benefits of diagnosis and early treatment (not waiting for disease to produce a diastrous disability before being recognized). In mental hygiene, of course, this was marked by the establishment of the Institute, — one of the original centers of its kind in the world, — and in the other fields of medicine by the Benjamin Franklin Clinic, one of the first group-practice clinics in America organized for comprehensive diagnostic service on a single-fee basis.

No one can dispute the brilliance of this record of service to medicine and to the public. But now, as I have suggested, you, in common with us all, are faced with major issues on whose settlement rests the future of not only this institution but the whole of medicine. What are these issues? What are some of the paths we might follow in seeking to resolve them? What in our history can teach us where to look for answers?

The basic issue, it seems to me, from the understanding of which will flow the solutions of nearly all the others, has been aptly phrased in the question "Whose medicine is it?" Shall the future role of medicine be developed primarily as a proprietary interest, or shall this role be the proper concern of all the people?

This question, I submit, was first answered in this country two hundred years ago today, when the charter of this hospital was granted. Final authority in the government of the institution was vested in the hands of a lay body, — the contributors, a group of distinguished and public-spirited citizens who in 1751 elected the first board of managers, also an unpaid lay body whose accounts were always to be open to public scrutiny. Here was established a fundamental principle — that although the professional aspects of the practice of medicine can be directed only by competent professional men, the ultimate responsibility for health protection is a public function. It is true that, according to Franklin, the idea of the hospital came from a leading physician, Dr. Thomas Bond, just as sixty years later the idea of a hospital in Massachusetts came from Drs. Jackson and Warren. In each case, however, when it came time to decide who should have final authority over the hospital, the physicians who had initiated the plans believed that this was properly a public rather than a medical responsibility. As a result, the legislatures of both commonwealths vested this authority, with the power to set standards for the kind of practice that should go on in the hospital and to appoint or discharge the medical staff, in a lay corporation and in its delegates, the board of managers (or trustees). In fact, although Thomas Bond was a member of the first board of managers here in 1751, when, a year later, the first temporary building was opened and the board wished Dr. Bond to become a member of the first medical staff of the hospital, he evidently believed that he could not properly accept this position while remaining on the board. So Bond, in a remarkable act of medical statesmanship, resigned from the board of managers.

Thus was first symbolized at this hospital the great principle that for the protection of its health the lay public must have the ultimate policy-making power.

Because hospital trustees and physicians are men of good will working together for a common goal, the need for exercise of the ultimate lay authority seldom arises. Yet it sometimes does, as when, almost a hundred years ago, the board of managers of this hospital, in what it conceived to be the public interest, required the staff to admit women medical

students to their classes, over the bitter opposition of most of the physicians of Philadelphia.

In America, of course, we see the same principle in many fields other than health. Our schools, our universities, our armed forces, our very laws and constitution are ultimately subject to public control. Medical institutions that, like this one, constantly seek to maintain the highest professional standards are enabled to function best in the public interest under the guidance of laymen. Where is a hospital owned by physicians or an educational institution owned by educators (medical or otherwise) that can be compared to the Pennsylvania Hospital or the University of Pennsylvania?

From the very establishment of Pennsylvania Hospital its board of managers took seriously its responsibility for professional standards. Any practitioner could apply for a position on the staff, but his credentials were most thoroughly scrutinized, and he was required to pass an examination by six members of the hospital staff, conducted in the presence of the managers. Moreover, the managers made at the beginning a rule that careful clinical records must be kept by the physicians — more than one hundred and fifty years before the American College of Surgeons made this a requirement for its approval. Unfortunately, as is regrettably the case in some institutions today, this excellent rule of the first board seems to have been for many years more honored in the breach than in the observance. Perhaps this was related to the fact that Franklin, a pioneer in scientific methodology as in so many other fields, left Philadelphia to become Provincial Agent in England a few months after the hospital opened its permanent building.

This, then, is the main issue we face: Is the public to continue to control the destiny of its own health? If, as I think we must, we answer this question in the affirmative, the answer follows to many another riddle that appears insoluble.

For example, what are the proper functions of a modern hospital? There is scarcely any topic in medicine over which voices can rise higher or tempers wax hotter. Is a hospital to be merely a kind of hotel for the sick to which physicians can bring their patients and treat them? Or should it be, as are the proudest hospitals today, a center for continuing the education of its staff, a focal point for the highest professional standards in the community? Beyond this, should it also expand its function to become a center for all the health services of the community, preventive as well as curative? Should it not be open to rich or poor, whether they are afoot or abed? If the public interest is the first to be served, one can scarcely imagine accepting anything but the latter alternatives.

As a matter of fact, Pennsylvania Hospital has long demonstrated its views on this issue. In its very first year, the question arose whether the hospital's services should be limited to bed patients. In a decision that has had enormous influence to this day, the managers insisted that ambulatory as well as bed patients be accepted for treatment. This was later extended for a time to include physicians' services and medicines for patients in their homes throughout the city. "Home care" provided from hospitals is a significant and spreading movement today, yet it was begun here in 1807. Should a hospital be limited to curative medicine or should it properly be interested in prevention, also? You answered that in 1808, when Pennsylvania Hospital gave public notice through the newspapers that "the Poor of Pennsylvania shall be vaccinated gratis, if they will call at the hospital." What about rehabilitation, the third phase of medicine about which we are all so enthusiastic today? In the very petition for your charter, much as in ours at Massachusetts General, by the way, appear these words: "Your petitioners beg leave . . . to present . . . that yet something farther seems wanting in Favour of such, whose Poverty is made more miserable by the additional weight of a grievous disease . . . (so that they) might again, by the judicious Assistance of Physic and Surgery, be enabled to taste the blessing of Health, and be made . . . useful Members of the Community, able to provide for themselves and Families." Moreover, from its first year, probably at Franklin's suggestion, this hospital had what we would now call "occupational therapy" in the form of "large and small spinning wheels and two pairs of cards, with wool and flax to employ such Persons as may be capable of using the same."

In short, home care, preventive medicine and rehabilitation, begun here so long ago, are necessary functions today and for the future in any teaching hospital that believes it should become a center of health service for its community.

However, for a hospital to be a center of health services raises another question that is even touchier. It is whether the expensive and first-class facilities and the well trained professional and associated personnel of a great teaching hospital shall serve, from the hospital, ambulatory patients of all economic levels. Traditionally, hospitals in America, although admitting rich and poor to their beds, have limited their ambulatory services to the poor. Recently, however, a notable change is taking place in this regard. It has become more and more apparent, as medical science has grown more complex, that medical service of high quality requires a team to perform it — a team of physicians of general and various special skills, of dentists, nurses, technicians, social workers, therapists and numerous others. For an individual physician to be able to surround himself with all these associates is virtually impossible. Good medical care today also requires complex and heavy equipment, such as few individual physicians could afford to purchase or could utilize if they had it for more than a fraction of its potential

capacity. What is more natural, therefore, than for a hospital, which already has this team and these facilities, to offer its services to ambulatory patients of all income groups? In this field, also, Pennsylvania Hospital has pioneered, first through your splendid doctors' office building and now through the Benjamin Franklin Clinic. It is, in my opinion, another function that, in the public interest, the staffs of all hospitals should look forward to performing, in association with their institutions. We at the Massachusetts General Hospital, in fact, hope once again to emulate the Pennsylvania Hospital in this respect.

If the hospital is, for the future, to be the kind of health center I have been describing, should it not cease to provide general medical service for its own surrounding area and limit itself to the highly specialized referred work that it and its staff are uniquely capable of performing? Some institutions have done this — and very brilliantly, but it seems to me that there is real danger of their becoming too rarefied, too removed from the realities of people's daily ills and problems. How can medical students really learn to be doctors in such an atmosphere? Much healthier, it seems to me, for a great teaching center, is a combined function of providing supervision and general medical care for even the most minor ailments of the residents of its neighborhood and of accepting referrals of more complex problems from a far wider area. In fact, one of the most significant developments now in progress among hospitals is planning for service on a regional basis, so that the smaller community hospitals and their staffs can benefit by regular visits of the specialists from a great center and in turn can refer to the center cases requiring highly specialized skills and facilities.

There is another, and very controversial, issue concerning the role of hospital service today. Is the staff of the hospital - health center we are envisioning engaged in unethical practice if the hospital accepts fees for professional services, such as for x-ray, laboratory and even clinical work, from its patients and pays its staff members by salary? The House of Delegates of the American Medical Association last summer decreed this to be unethical. To the average layman, this controversy is confusing. Are physicians not permitted to function as professional men when they are paid by salary? Most of our prized scientific discoveries have been made by salaried physicians and allied scientists. Are the professors at our medical schools incompetent physicians if they are on salary? Is something wrong with the winners of the highest scientific and professional honors in this country or in the world if they do not charge fees for their services? Last week the entire salaried clinical faculty of the Yale University School of Medicine was cited as "unethical." Does this make sense? What about the salaried staffs of our great clinics or of the Henry Ford Hospital or the University of Chicago? The salary issue itself appears to be inconsequential. The real issues, it seems, are: first, whether the compensation of salaried physicians is adequate (I, for one, would agree that it often is not) and secondly, whether the competition offered by such a salaried hospital staff is unfair to other medical practitioners.

In reality this comes close to the heart of the main issue first mentioned; that is, "Whose medicine is it?" A little common sense applied to this issue, with the public participating, would, I believe, quickly resolve it. Salaried physicians must be adequately remunerated; competition with other practitioners is not unfair if a high standard of service to the public is thus achieved. Too frequently this issue has been regarded as something to be dealt with solely by the physicians and the hospitals. Like the others we have mentioned, however, this too must ultimately be settled on the basis of what is best for the public.

Seen in that light, it appears that compromises can be found through which all could agree that there is nothing unethical about a salary as such but that it is unfair for a roentgenologist, for example, not to be treated with the same professional respect and dignity as a surgeon — that for an institution to "profit" handsomely from fees for professional services is exploiting not only the physician but also the patient.

So much for the opportunities and problems of the service functions of a hospital. As you are well aware, hospitals like this one have two other vitally important functions; teaching, so that we may be able in the future to continue to render the high standard of service of which we are so proud, and research, so that we may improve the effectiveness of our service and our teaching.

Hospitals can, — and many do, — give excellent service without engaging in teaching or research. But such hospitals, must of course, depend on the leadership of institutions like this one that do carry on these activities. It is fair to say, I believe, that no hospital can be a truly great leader in medicine without teaching and research. The staff that does not have the stimulus of instructing others and seeking out new areas of knowledge can hardly be expected to keep in the forefront of medical progress in these days of rapid movement.

If teaching is to have its most valuable influence, it seems to me, it must include the teaching of both graduate and undergraduate medical students — as the Pennsylvania Hospital and the Massachusetts General have evidently thought since their beginnings. Without undergraduates, teaching can too easily depart from the problems of patients as persons and restrict itself to the thin air of "scientific medicine." Important as technical discoveries are, they can never, in medicine, be a substitute for the personal understanding of the physician. Without the teaching of residents, fellows and other post-

graduate students, on the other hand, the borders of scientific achievement will never be advanced. We must have both, if we are to call forth the best a hospital staff can give.

Medical research, also, can best be carried out in close relation to patients, especially research on the chronic diseases like cardiovascular disease, arthritis, cancer and mental illness, which are our greatest health problems today and which either cannot be produced in animals or take so different a form in them that findings cannot easily be applied to man. Of course, a hospital, where all the varied skills and facilities of modern medicine are assembled, and where the patient can be properly protected and systematically observed, is the ideal location for research of this type. However, if research is to yield fundamental truths, the basic sciences of chemistry, physics and biology must also be associated with the hospital — else we can expect only the more superficial, though often useful, results that purely clinical methods permit.

Up to now, I have discussed principally the question of the proper functions of a hospital, particularly a teaching hospital, today and for the future, and I have tried to discuss it in the light of the public's interests. Other large questions confront us that should also be touched on.

Most obvious, perhaps, and certainly one of the most disturbing, is the financial crisis of the voluntary hospital. Last week I heard that a Boston hotel manager had said that he could run the Massachusetts General Hospital at a profit — so why couldn't we? I don't know whether he really said it or not, but if he did I heartily agree with him. Certainly we could function at a profit, but what would it mean? Principally, it would mean lowering our professional standards and closing our doors to all who could not pay the full cost of their care with, naturally, a suitable margin of profit. Is that what we want to happen in our hospitals?

As a matter of fact, this has been done in some parts of the country by the simple device of establishing one set of hospitals for those who can pay full cost and a separate set, under Government subsidy, for those who cannot. It solves the financial problem, via taxes, but is it a good idea? Personally, I don't think so; there should be only one kind of medical care for all — good medical care. Surely this is more likely to be accomplished if hospitals in general, be they voluntary or governmental, serve a broad cross-section of the community, with both charitable funds and taxes used to pay for the care of those who cannot pay for it themselves. With regard to payment through taxes, Pennsylvania Hospital has had experience dating back at least to the Revolution, when it had the greatest difficulty in securing payment for the care of hospitalized soldiers, both American and British. Furthermore, on at least one occasion, in 1790, the board of managers found it necessary to take legal action to recover a large sum of money that was owed by the City of Philadelphia for the care of the poor from the Almshouse. They collected, too. Perhaps we can learn something from this today.

That brings me to another question, namely, what is the proper role of government in the provision of health services? Here, too, the Pennsylvania and Massachusetts General Hospitals have an example to offer. Each of these hospitals was established by an act of the legislature, and each received generous aid from tax funds in erecting its original building. Indeed, in Philadelphia, Franklin devised a formula that is so close to that of our recent Federal Hill–Burton Act as to be startling. You will recall that in your original act, drawn by Franklin, the legislature promised £2000, provided that an equal amount was raised by public subscription. The only difference between that and the first Hill–Burton formula is that under the Hill–Burton Act public subscription has had to raise two thirds rather than one half of the cost. One half the cost of the new Research Building at Massachusetts General Hospital came from the National Institutes of Health of the United States Public Health Service. One third of Massachusetts General Hospital's annual research budget is supported by Federal or State agencies.

This current tax aid, like that given here so long ago by the Colonial legislature, has not meant and need not mean Government domination or political control, nor does Federal aid to medical, nursing and other professional education need to mean these things — or payment of hospitals by government for the cost of the care of the needy. The proper role of the Government, like the other issues discussed, if viewed dispassionately in the public interest, can, I am convinced, be resolved by men of good will.

What about payment for medical care in general? The same principle of public participation applies here also. That insurance is a valuable method of enabling people to pay for hospital care and doctors' services no one denies today. Should this be voluntary or obligatory insurance? Isn't this another matter to be settled in the way that best meets the health needs of the public? Our voluntary insurance plans have accomplished much we can be proud of, but many persons who want and need such insurance still do not have it. Voluntary methods may reach them all eventually. On the other hand, can we be so positive that obligatory insurance is synonymous with state socialism? Is Workmen's Compensation or obligatory automobile insurance socialism? Mind you, I am not here advocating obligatory medical-care insurance. I am, however, strongly advocating reasoned public discussion of this issue, along with the others, rather than shouts and battle-slogans from every side.

Actually, it seems to me that a more fundamental question than whether medical-care insurance should

be voluntary or compulsory is what standards we should demand of any medical-care insurance. Just now, most of our voluntary insurance is fragmentary, often leaving the patient to pay much of the bill from his own pocket. Even less desirable, from the standpoint of the public health, is the fact that, unlike your board of managers, most insurance plans show no effort to improve professional standards. In a few exceptional instances, mostly when lay boards of trustees rather than physicians control the plans, high professional standards for participation, comparable to those set by your managers for professional staff appointments at this hospital, have been established.

Another problem is created by the fact that most existing insurance is limited to payments toward the cost of hospital care and physicians' services in the hospital. How does this promote the preventive medicine, early diagnosis and treatment for which this institution is distinguished? Are we not influenced by this limited insurance to use our hospitals more than would be medically necessary if preventive and diagnostic services outside the hospital were also covered? In turn, this may mean, it seems to me, that we are providing, at great expense, more hospital beds (at least in some communities) than are really needed. These and many related issues deserve much public as well as professional consideration and much thoughtful experimentation if they are to be resolved for the best interests of us all.

Unfortunately, experimentation in various types of voluntary medical-care insurance, especially those associated with group practice and lay control, and trials of various types of hospital-full-time-staff relations, have been seriously hampered, in many instances, by the bitter opposition of medical societies. By threatening loss of society membership and possibly of hospital staff appointments, some societies have put physicians interested in such experimentation under strong pressure to abandon it. Indeed, laws designed to prohibit experiments in either of these fields have been adopted in many states at the instance of medical societies. This is hardly the statesmanship of Franklin or of Thomas Bond.

Here, it seems to me, we have compulsion in its most destructive form. How are we to learn the methods best designed to provide the public with medical service of high quality if we are forbidden to experiment? Surely this kind of prohibition is the exact antithesis of the scientific method of which we physicians boast — and of the system of free enterprise for which this country stands. To reverse this trend and restore freedom the people must play a leading role. Only by their action, in collaboration with the medical profession and its associates, can the nation, — or indeed physicians themselves, — be made free to serve in the best interests of the health of us all.

As one of the leaders whose aid will be sought in deciding these crucial and difficult issues, the Pennsylvania Hospital has shown, recently as in its splendid past, courage, initiative and wisdom. The years ahead are a challenge, but a challenge that your tradition and your energetic spirit have superbly equipped you to meet. We shall continue to look here, as we have looked for two hundred years, for the strength, imagination and medical statesmanship that have so brilliantly illuminated your past. I am confident that we shall not be disappointed.

PSYCHIATRIC ASPECTS OF CEREBRAL ARTERIOSCLEROSIS*

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THAT physicians with varied disciplines of observation, training and therapy should be invited to discuss cerebral arteriosclerosis before this society is of timely significance. The Federal Security Agency[1, 2] reports that chronic diseases are the leading causes of death in the older age groups. In 1900 they were also the leading killers of persons sixty-five years and over. Then, as now, heart disease headed the list. Intracranial lesions of vascular origin were the second leading cause of death in 1900 and the third in 1948, with cancer and other malignant tumors now assuming second place. But the percentage distribution of deaths from intracranial lesions of vascular origin for persons sixty-five years or over has shown a slight increase over this period from 12.2 per cent in 1900 to 12.4 per cent in 1948.

When we think of arteriosclerosis and of vascular lesions our first thought is of the heart, but the time has come when we must think of the brain as well. In 1947 Rothschild[3] reported that senile psychoses and psychoses with cerebral arteriosclerosis accounted for 33.7 per cent of all first admissions to the Worcester State Hospital in the year ending June 30, 1945 — an increase over preceding years. Dayton,[4] in his statistical study of 1940, showed that there was a marked increase in admission rates to Massachusetts mental hospitals from 1917 to 1940 for psychosis with cerebral arteriosclerosis. In this group men showed higher admission rates than women. In the senile group the women presented the higher admission rates. While the senile group was decreasing, the arteriosclerotic group was increasing so markedly that the psychoses of old age in general were showing a definite rise and becoming the leading problem in psychiatry. Kolb[5] has estimated that if present admission rates and population trends continue, we may expect by the year 1980 an increase of 200 per cent in the number of first admissions to state mental hospitals for the mental diseases associated with old age.

Many investigators believe that the etiology of cerebral arteriosclerosis remains speculative, but recent psychiatric studies, as will be indicated later, suggest that heredity and tension contribute at least some influence in causation. Little has been done to correlate personality studies with organic disease. However, many inferences and unsubstantiated concepts have been proved erroneous by the reports of Gellerstedt[6] and others that comparatively advanced changes, particularly of the type found in the senile psychoses, can also be demonstrated in the brains of well adjusted old persons. With this as a starting point, a new conception of senile and arteriosclerotic psychoses was advanced when recent researches on these disorders by Rothschild[7-11] revealed a frequent lack of correlation between the severity of the mental disturbance and the extent of the cerebral damage. These observations suggested that cerebral alterations might not be the only etiologic factors in senile and arteriosclerotic psychoses but that psychologic factors might exert an influence on their origin. In certain cases worry, anxiety over failure of health with advancing years, financial hardships, loss of relatives, personality defects and the like seemed worthy of attention. Thus a new method of approach was indicated, as something can be done about such factors. Psychiatry has worked out methods that can help in solving these personality problems and lessening such mental conflicts. It is important to study these aging patients as persons who break down because of two complementary sets of factors — personality problems and degeneration of brain tissues. Stressing the former will often produce surprisingly effective results.

In a clinical approach to the understanding of cerebral arteriosclerosis we must first try to distinguish between cases with and without psychosis and also between the psychoses with cerebral arteriosclerosis and the senile psychoses. These conditions merge into each other, and sharp differentiations are frequently impossible. Often there is found in the elderly psychotic a perplexing mixture of both functional and organic symptoms associated with cerebral arteriosclerosis and senile dementia. The functional element is significant in the establishing of a favorable prognosis. Another complication is that in diseases of the nervous system a limited number of symptoms are often indicative of many different clinical syndromes. Agitation, anxiety, worry, confusion, loss of memory, emotional instability, irritability, sudden explosive outbursts of unreasonable laughter or anger, delusions, hallucinations, tremors of the hands and face, thick speech, head noises, vertigo, generalized weakness and unsteady gait are significant examples. These symptoms in and of themselves are pathognomonic of no one clinical entity. It is the way they are grouped into syndromes, the timing of their onset, and the rapidity or evolution of their development that are important.

First let us consider the cerebral arteriosclerotic without psychosis or with no evidence of even a

*Read before the Section of Neurology and Psychiatry of the Massachusetts Medical Society, Boston, May 24, 1951.

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transient episode of thrombosis of a small intracranial artery. These patients do, however, offer clinical evidence of a slow, gradual diminution of the blood supply to the brain. The first manifestations are likely to occur after a sudden change or even an anticipated change in their accustomed pattern of daily activity. They generally occur sometime after the age of fifty, although arteriosclerosis may occur at any age. In progeria, for instance, growth almost ceases within a few months to three years after birth, and subsequent senile-like changes occur, with reported calcification of the arteries and severe mental defect.

In the aging person the first symptom is often fatigue and an associated loss of interest before or shortly after retirement. It may follow moving into a different locality or the loss of a loved one, money or social or professional prestige. Powers of prolonged concentration diminish, especially in any new activity. Another common symptom is normal activity in the forenoon and dozing in the afternoon or early evening in a patient who formerly had been alert and interested throughout the day. Such persons have a remarkable ability to awaken at the slightest stimulus, to be immediately alert, to accurately infer what has transpired while they were asleep and to continue efficiently as before. The placid can usually control their irritability, but the more dynamic are given to sudden explosive outbursts of anger, only to apologize immediately. They are aware that something is wrong but loath to mention it to others. Often they are silent worriers, with one-track minds that have made them successful in their chosen professions, but without inner resources or an avocation. Their blood pressure is usually somewhat elevated, averaging 170 to 190 systolic and 80 to 100 diastolic. They may still function in advisory capacities, make out their income-tax forms or even drive an automobile across the continent. They may gradually develop more objective symptoms or suddenly die of cerebrovascular hemorrhage.

Among those with more advanced neurovascular disease, we have the group subject to what Alvarez[12] calls "the little strokes." This group is apt to be intermittently psychotic in a manner obvious to a careful observer. They spend ten to twenty years dying, gradually fading out with cerebral arteriosclerosis and occasional episodes of thrombosis of a small intracranial artery. These episodes are seldom recognized as manifestations of a long-lasting, eventually fatal disease. Because of its chronicity the course of the illness can be observed adequately only by the victim's relatives or long-time friends. The first episode may come in the forties or even in the thirties; it frequently occurs unobserved during sleep. A sudden change in character and ability makes the diagnosis relatively easy, although this symptom may be interpreted as an unexplained nervous breakdown. The patients' social or physical inadequacy may preclude any further remunerative employment. A psychologic disorder may develop, characterized by moral deterioration, indifference to personal appearance, undue emotional lability or a state of agitated depression, making the patient a difficult problem in the home. A fall, attributed to tripping, may be due to a momentary loss of consciousness. Cerebral disease may cause them suddenly to be unable to sleep.

The subjective symptoms are eventually, either slowly or suddenly, augmented by neurologic signs. Many patients suffer with sudden distress in the thorax or abdomen, often attributed to "acute indigestion" but apparently referred from the brain. Indigestion due to muscular spasticity of the digestive tract may esue. Vertigo is common. The clinician should watch for a slight bulbar paralysis, a Parkinson syndrome or paresthesias and numbness, as well as a slight weakness of muscles, significant loss of weight, a burning sensation or a bad taste in the mouth, a facial pain, sudden blindness or arthritis in a weakened extremity.

Knowledge of these "little strokes" is rarely the result of direct observation by the physician but is usually obtained through careful questioning of the relatives or business associates who alone have been aware of the sudden aging or abrupt change in the character and ability of the patient. Frequently a marked drop in blood pressure occurs immediately after one of these small thrombotic cerebral traumas.

The prognosis is often better than might at first be expected. Although it is sometimes hopeless, patients may live for years without another episode and may even continue some form of remunerative work. These patients require careful observation because of their tendency to be intermittently psychotic. Under stress or strain they tend to become confused, irritable and even delusional, and show poor judgment. They may even show diurnal variations of insight and judgment according to the efficiency of the cerebral vascular structures and the resultant amount of blood supplied to the brain at the moment. Therefore they may be lucid and aware of their environment at one hour of the day and confused, delusional, suspicious and even paranoid at the next. Consequently it requires judgment and insight based on years of experience to determine their legal and social status in the community and also whether they are capable of understanding a business transaction or of making a valid signature. It is in such matters that psychiatric help is advisable. Frequently paranoid trends are associated with organic brain disease; in the cerebral-arteriosclerotic patient these can often be of a subtle and embarrassing nature. Various practical problems arise. Allen and Clow[13] have pointed out that the cause is often not recognized until after the patient's accusations have received credence and unfortunate situations have occurred. These paranoid delusional symptoms frequently represent the

first evidence of beginning organic brain disease. The victim may build up a defense against his own feelings of helplessness and frustration, recognized by him long before they become apparent to others. His delusions of persecution may even cause him to take court action. Such action is sometimes directed toward members of his family, who from intimate observation recognize the necessity of treatment and seek his admission to a mental hospital. Wills may be changed because of delusional beliefs of the patient; these are often, with justification, contested by the original beneficiary. The question of the mental competence of such persons requires scrupulous consideration and a careful review of the facts in addition to psychiatric insight in such situations.

Cerebral arteriosclerosis may also weaken the usual inhibitions imposed on one's instinctual desires in much the same manner as does alcohol in the incipient stages of acute alcoholism. The organic impairment often relases the control that is exerted over latent sexual urges when the brain is functioning adequately. Such patients are often accused, doubtless in some cases justifiably, of corrupting the morals of minors, but it may be the youth who exploits the aged person. The cerebral-arteriosclerotic patient may be induced to make a disastrous marriage with an unscrupulous, usually younger, member of the opposite sex; not always with impunity, however, for there is the case of the woman who married an elderly arteriosclerotic who suddenly exclaimed to her, in a polite gathering, "Shut up, you God damn fool!"

Doty[14] has pointed out the physiologic and psychologic factors that predispose the older person to delirium. He points out that prolonged recumbency, contributing to circulatory stasis, is an important factor. Perception is not as prompt and its span is not as long in the old as in the young, facts that may contribute to a tendency to misinterpret environmental stimuli so that visual and auditory illusions develop more readily. Doty advocates the early recognition of a developing delirium in order that sedatives or other drugs that may be responsible may be discontinued. Hydrotherapeutic measures or other non-drug methods of securing rest and sleep for the patient should be instituted. Treatment to promote excretion of drugs and waste products through the skin, kidneys and bowels should be prompt. Avoid confusing or puzzling treatments and explain all necessary ones. Also, reduce all possible external stimuli by refraining from changing the patient's location and having as few physicians and nurses caring for him as possible. Exclude all visitors and keep him under constant observation. Confusion is thereby markedly reduced. Proper nursing supervision is the most important of all.

Patients whose basic personalities have shown such features as sensitiveness and a tendency to suspiciousness and jealousy may display prominent delusions of persecution during a delirium and may only partially recover from them with the subsidence of the delirium. Sometimes the delirium seems to have released personality features that do not disappear with recovery from this acute mental disturbance. However, in many cases, with the prompt withdrawal of sedatives, proper fluid and nutritional intake and adequate elimination, the delirium subsides in a period of a few days to several weeks with a return to as great a state of efficiency as before.

Evidence of cerebral arteriosclerosis does not usually present any serious complication. In the psychotic patient with cerebral arteriosclerosis the symptoms are in keeping with what we would expect when there are either gradual or sudden changes in the amount of blood that reaches the tissues of the central nervous system. Rothschild[15] has enumerated them in greater detail than other investigators and has differentiated them, as far as it is clinically possible, from the senile psychoses. It should be remembered that his studies are based on case material obtained from patients, mostly committed to a state mental hospital. The emotional picture in cerebral arteriosclerosis is a more varied one than in senile dementia. The physical manifestations are more pronounced, and there may be periods of loss of consciousness alternating with or followed by periods of amazing lucidity. The process is a more reversible one than that in senility, in which the symptoms are associated with a progressive and more or less slow alteration or degeneration in the brain tissues themselves.

In a psychosis associated with cerebral arteriosclerosis there are likely to be prodromal or early symptoms associated with a variation in the pressure and alteration in the amount of blood in the cerebral arteries. The most common prodromal symptoms are headaches, dizziness, vague somatic complaints and a more or less prolonged period of physical or mental letdown. Apoplectiform or fainting attacks, symptoms of cardiac decompensation and, less frequently, convulsive seizures often precede the mental symptoms, although these physical phenomena may occur at any time during the course of the disease.

Although the mental symptoms may be sudden or gradual in development, a sudden attack of confusion is noted in more than 50 per cent of the cases; the neurologic symptoms often predominate. The patients show marked clouding of consciousness, complete loss of contact with their surroundings, incoherence and pronounced restlessness. Hallucinations may be added to produce a delirious picture. In some cases there are few, if any, premonitory mental symptoms, but as a rule the onset is preceded by a gradual reduction of physical and mental capacities. The fact that it occurs in the younger as well as in the older patients suggests that it is really the first indication of an insufficiency

of the cerebral circulation. Occasionally the mental letdown may exceed the limits of normal; hence it would be more accurate to speak of an insidious onset with an acute outbreak of more overt psychotic disturbance.

When the onset is gradual, the mental disturbances are similar in many respects to those observed in senile dementia. There is a gradual intellectual failing, manifested by a loss of efficiency, impairment of memory and the like. The patient may display a lowering of moral standards and irritable, aggressive and quarrelsome behavior. Subjective complaints, such as weakness, fatigue, uneasy feelings and unpleasant somatic sensations are frequently noted. Depressive feelings, emotional instability and a fear of impending failure, with physical and mental inadequacies, are often prominent features; frank suicidal tendencies are by no means uncommon. Explosive outbreaks of weeping or laughter are occasionally encountered, usually in cases with gross neurologic alterations. Transient persecutory ideas or jealousies may be observed, but persistent, well developed paranoid ideas are rarely observed. Delusions and apprehensions appear more frequently in the evening, often interfering with sleep. The impairment of memory tends to affect recent rather than remote impressions but is apt to be spotty rather than diffuse. Fabrications are occasionally noted. Although judgment is impaired, this seems dependent on the efficiency of the cerebral circulation at the moment. There are periods in which even the psychotic cerebral-arteriosclerotic patient may show lucidity and insight, understand a business transaction and be capable of making a valid signature. Such periods should be accurately recorded by competent observers in the case histories of these patients.

Beckenstein and Gold[16] studied 100 consecutive patients with senile psychoses and 100 consecutive patients with psychoses with cerebral arteriosclerosis who were admitted to Brooklyn State Hospital from April to June, 1943. The study showed that the total duration of mental illness in the senile psychotic patient tended to be one to three years, and that in the cerebral-arteriosclerotic psychotic patient the total duration is generally less than two years. The cerebral-arteriosclerotic psychotic patients had a greater chance of survival; when well enough to leave the hospital they were generally discharged within two months. In the senile psychoses the type of onset was not of much significance, as the disease was progressive and the outcome was the same whether the onset was acute or insidious. The greater frequency of the acute onset among the cerebral-arteriosclerotic group was demonstrated by the fact that 77 per cent had this type of onset, which corresponded with Rothschild's findings and seemed of some value in determining the prognosis. These authors noted that Sands,[17] in a previous study of cases of cerebral arteriosclerosis with confusion due to infection, found that with proper treatment of the infection recovery from the confusion occurred within one to three months.

Clow[18] in 1939 made a detailed study of 100 patients suffering from psychosis with cerebral arteriosclerosis who were treated at the New York Hospital–Westchester Division. He noted a high incidence of familial cardiovascular renal disease. Fifty-five of the 100 patients had a family history of cardiovascular renal involvement; 51 of them had a family history of cerebral arteriosclerosis as manifested by cerebral accidents. There was severe cardiovascular renal disease in 1 parent in 36 cases. The members of the families were predominantly tense, energetic and aggressive. Manic-depressive psychoses were prominent in the family histories. The patients also had frequently had affective psychoses. Many of them suffered from peripheral and retinal arteriosclerosis with hypertension. Fifty had a history of vascular accidents; 59 showed focal signs. Precipitating emotional factors were noted in 76 cases, the most common of these being the illness or death of a close relative or friend. The toxic effect of drugs contributed to the psychotic symptoms in 37 patients. Treatment necessitated a knowledge of both psychiatry and internal medicine. Adequate fluid intake, easily digestible food, enemas, massage, baths, packs and proper rest were helpful at first. These were followed by the stimulation of the interests of the patient and the awakening of new ones. He was encouraged to make friends and to follow a prescribed routine of physical activity and occupational therapy in keeping with his capacities. Reassurance and teaching the patient to be content to live within his limitations were beneficial. It was also equally important to educate the patient's family concerning his condition and how to modify his environment when he returned home.

Under the treatment outlined above, 11 of the patients recovered from their psychosis, 5 with slight residual memory defects. Twelve were much improved, 31 were somewhat improved, 30 were unimproved and 16 died. What is especially significant is that 49 of the 100 patients were able to return to their homes. This study shows what can be done in a private mental hospital under excellent conditions of care and therapy. It should also be remembered that these patients were economically and socially equipped with adequate resources and accommodations for subsequent home care. The study strikes an optimistic note by showing that in psychotic patients with cerebral arteriosclerosis a functional reversible element may be present and that under suitable conditions a certain percentage of them recover.

Subsequent studies at the New York Hospital–Westchester Division have revealed that a systematized routine, with proper nursing care, adequate nutritional intake and proper elimination,

frequently conduces to a state of adjustment in which the patient can function comfortably without supportive drugs, sedatives or special diets. Many patients come to the hospital suffering from psychoses with cerebral arteriosclerosis who have been taking barbiturates, aminophylline, paraldehyde and Demerol and have been on low-protein, salt-free diets. Within a few days all these aids can, in most cases, be discontinued.

There are many reasons for this. When such patients are cared for in their homes or in a general hospital, if they are noisy they at once attract attention and awaken apprehension. It is often expedient for the welfare of others to quiet them as quickly as possible. At home, the physician rarely visits them oftener than once daily, and the nurse is frequently on twelve- or twenty-four-hour duty. Sedatives lessen the work of both physician and nurse. In a general hospital both physician and nurse have to meet the criticisms of other patients and relatives. However, in a mental hospital with adequate personnel, someone is always available who can talk quietly with the patient and exert a personal influence. In an adequately staffed mental hospital the personnel can relieve one another; hence the physician, nurse or attendant in charge of the patient can approach him fresh and relaxed and thus not unfavorably influence the patient with personal tensions, anxieties, or irritations resulting from his own accumulated fatigues. Furthermore, the personnel of a mental hospital see and treat such patients constantly and are not merely confronted sporadically with isolated cases; they thus have an assurance and confidence that the patient is quick to appreciate. Having the patient under constant twenty-four-hour supervision enables the personnel to ascertain quickly whether their methods are producing a favorable result or not. It takes courage to know when to refrain from prescribing for the patient. Keeping the patient under unobtrusive surveillance is desirable, but we must all at times curb our professionally conditioned impulses constantly to do something for or to the patient.

Sometimes digitalis, Demerol, morphine, aminophylline or paraldehyde, is indicated, but such medications should be discontinued as soon as possible. The advisability of medication is checked by continuous clinical observation and laboratory studies. The orders for any medication are written daily; standing orders, which are likely to be continued for indefinite periods, are prohibited. Special diets are likewise sometimes necessary, but these are discontinued as soon as possible after adequate clinical observation and suitable laboratory studies of the blood and urine.

For elimination, simple cathartics like milk of magnesia or cascara with mineral oil are usually sufficient, but they should be discontinued as soon as possible or at least used intermittently. In the arteriosclerotic patient the lower bowel is often sluggish and lacking in muscular tone. The need for enemas should be determined by rectal examinations by the physicians rather than by the statements of the patient or the nurses. Usually a low enema once or twice a week, preceded by an oil instillation, is sufficient. Often a clear return from an enema is reported; this may be due to canalization of the fecal material by the enema tube. In a rectal examination the walls of the rectum or descending colon should be carefully palpated. The depleting trauma of colonic irrigations should be avoided.

In a consideration of electric-shock therapy for the cerebral-arteriosclerotic patient, Prout, Allen and Hamilton[19] have pointed out that although it is not indicated as specific treatment it is a relatively safe procedure in skilled hands for many complicating emotional disorders of these patients. Its use is indicated where there is a complicating mental illness, fundamentally functional in nature.

Under functional stress, elderly patients may display symptoms such as confusion, disorientation and gross memory defects, which are presumably of organic origin and which may be alleviated or may disappear with recovery from the depression. Patients with a psychosis due to arteriosclerosis in whom evidence of cerebral damage is not marked and who are deeply depressed often benefit from electroshock therapy, which relieves the depression. But the cerebral-arteriosclerotic patient should first have the opportunity to respond adequately to the usual more conservative methods of psychiatric therapy.

A careful survey of the adequacy of the cardiovascular system is essential. Hypertension, abnormal electrocardiograms, a history of angina pectoris or coronary thromboses and inactive rheumatic heart disease with valvular lesions are not in themselves contraindications to electric-shock therapy. A patient whose cardiac reserve enables him to walk 100 yards without obvious distress is able to stand electric-shock treatment. Added assurance is given when the muscular response is modified by a curare derivative. Agitation and excitement of themselves may put more strain on the heart than the electrically induced convulsion.

The use of a curare derivative prior to electric-shock treatment, when carefully administered by trained and experienced physicians, is a safe procedure with the cerebral-arteriosclerotic patient who has no gross neurologic symptoms or history of recent cerebral thrombosis or hemorrhage and whose electroencephalogram reveals no evidence of serious brain disease. The curare derivative can be safely given in such doses as are necessary to prevent any true convulsive reaction (clonic or tonic muscular responses), allowing only isolated fibrillary twitchings that are not capable of changing the position of the extremities. Such curarization should never be employed when adequate resuscitative equipment is not immediately available.

Discussion

The symptoms of cerebral arteriosclerosis are so varied and complex that any attempt to use illustrative case material is difficult, as no one case or small group of cases can exemplify all the problems involved. Most symptoms are manifestations of cortical damage. Often the patients, on superficial observation, make a favorable impression that is not borne out by a more detailed study; at the same time, what might seem as trifling alterations in the life patterns of these patients are sometimes of profound prognostic significance.

Case 1. A sixty-five-year-old married man came to the psychiatric out-patient clinic of the New York Hospital (the Payne Whitney Clinic) complaining of headaches, hot flashes and periods of sudden uncontrollable irritability (he admitted that he had pushed his wife). He had retired about a year prior to admission on a small pension, after having held various positions throughout his life, including the tending of bars in hotels and night clubs. He was depressed and aware of needing help and was willing to accept hospitalization. Gastrointestinal-tract x-ray films a few months previously had been negative. The gist of his complaint was as follows: "I imagined I had cancer, duodenal ulcer and like things. Get despondent, think of ending it all. I would do anything to stop it. I guess it is the devil tempting me. I get one spell a day. Right now I have butterflies in my stomach. When I retired, I was all in. Now it is right over the eye-balls. My eye-balls feel as if they are on fire. There is an empty feeling in my head. I get hysterical at times. I cry. I also get irritable. Got irritable with my wife and gave her a push the other day. I was sorry afterwards. My heart beats terribly at times. Pounds in the head. Like someone not there and pounds at it. I didn't want to be alone. I didn't seem to be getting anywhere. I had terrible headaches today. I take aspirin. Don't help much. The devil is after me when I am weak. Tells me to commit suicide. I read in the papers where a doctor, a surgeon, committed suicide. My son showed it to me. He shouldn't have. I get peculiar sensations and pain in my head." He mentioned his son's critical attitude: "Well, father, you are retired. The city has let you down. Stop complaining. Go get a job. You have got to be digging ditches or something. Don't be fussy. I see men downtown in their seventies shining shoes. I don't ask you to do that." The patient continued: "I get hysterical. I get crying spells. When I go to bed at night I feel better. I lay down for 40 minutes and slept. When I got up, I felt fine. My wife says, 'I don't think that lying down does any good'."

The patient had days when he felt fairly well and days when he had headaches, was dizzy and became restless, fearful and irritable, taking eight aspirin tablets a day. He wanted to sleep all the time. He was considered to be suffering from cerebral arteriosclerosis on the basis of his variations of mood and attention; at some times he was more lucid than at others but was often forgetful. Depressed about the future, he often wanted to do something rash but did not want to hurt others. He definitely needed supervision.

A short time later the patient obtained a part-time position sweeping, cleaning toilets and occasionally tending bar in a nearby café. He returned to the clinic smiling, where he had frowned before, and looking ten years younger. For about forty-five minutes he was able to talk about his job and his two sons without directly referring to himself. He continued, "It's January. Got to expect that. My head has been clear 75 per cent of the time. Had a wonderful Christmas. I prayed and prayed so as to have a good Christmas and not be a burden to others. Oh, yes, I think the job has done wonders. One important thing, I have practically eliminated aspirin. I had a good time New Year's Day. My sister-in-law said, 'You look like your old self.' I have worked every day, seven days a week."

This presentation shows the importance of a job or some form of occupation after retirement. The patient, who was becoming increasingly distressed at home, where he was getting on the nerves of both his wife and son and whose distress was increased by his family so that mental hospitalization was seriously considered, may be considered recovered.

Attention to details is especially important in establishing the diagnosis and in determining the degree of efficiency and the results, if added emotional stress or responsibility of adjustment is suddenly imposed.

Case 2. A patient was admitted to the New York Hospital–Westchester Division with a left hemiparesis and a paranoid attitude toward his wife. He was co-operative and appreciative. He enjoyed physiotherapy and the occupational period. He was able to spend most of his time writing a novel and a religious pamphlet, and he socialized with the other patients. He ate and slept well, but he was tense and smoked excessively. His speech was circumstantial and tended to be repetitious. An accomplished writer, he occasionally used the wrong word without seeming to realize it — for example, "neurosis" for "neurologist." He denied depression, anxiety or fear, but admitted he was "afraid of losing out" after his stroke. He was evasive in talking about his present illness and gave a disconnected story of its onset. In talking with the certifying physicians (whom he called police detectives in a joking manner), he admitted that he thought all the doctors and nurses were sexually intimate, that he thought his wife had been indiscreet and that he had threatened her with a poker. When these subjects were not directly brought up, he emphasized his love for and trust in his wife.

Although he appeared correctly oriented for time, place and persons, he made an error in the test for retention and immediate recall. He did poorly with the interest and algebra problems, not realizing his obvious mistakes. He interpreted the test story well but concentrated poorly on the attention tests, making five omissions in the auditory test, which had to be made slowly. He was on the defensive about the memory test and the repetition of digits, basing his refusal to do them on being tired and sleepy. His intelligence, previously superior, was impaired. His insight was poor, but his judgment, especially about extrapersonal matters, was fair. Later any emotional frustration, such as not being allowed home for Christmas, brought his usually latent suspicious trend to the surface.

Rashkis[20] has revealed that the behavior of selected groups of schizophrenic, general paretic and cerebral-arteriosclerotic patients on sorting tests that utilized words and numbers on manipulated objects indicated that the three types of patients tended to be behaviorally distinct from one another in a statistically significant manner. The cerebral-arteriosclerotic patients tended to perform in an "unco-ordinated" manner that was statistically no different from that of the general paretics, but unlike the latter they showed awareness that their performance was inadequate. Schizophrenic and cerebral-arteriosclerotic patients performed generally in a significantly different manner but were alike in that they both tended to display some critical evaluation of their behavior. The thinking disorder of the cerebral-arteriosclerotic patient was interpreted as a deficit in performance potentialities; the factor of intellectual organization was essentially unimpaired.

The following description of a cerebral-arteriosclerotic patient with a serious organic impairment

discloses retention of some of these intellectual faculties.

CASE 3. The patient was amiable, co-operative and more alert than at first appeared. He smiled persistently and registered interest in and acceptance of his environment. He ate and slept well and took an interest in his appearance. His talk showed evidence of dysarthria and a predominantly motor dysphasia. He appeared to hear and generally to understand what was said to him but had difficulty with his verbal replies. He had to enforce his remarks with associated movements of his arms and hands and manifested perseveration and euphoria. When he talked quickly, without much initial conscious effort, words came out, almost explosively but clearly, but when he endeavored to think before speaking and to recall associations, he mumbled incoherently, with limited flexibility of the oral muscles and vocal cords. He did not stammer or stutter. For example, when asked his name, he said, "My name is —," saying it correctly. As he did so he raised his right arm, extended his forefinger and tried to write his name in the air, spelling it aloud as he did so. He repeated it several times. He was childishly contented and appreciated attention. At first he was confused about the location of his room, but he soon learned its location. When he wished to take anyone there, because of his difficulty in speaking he would take him by the hand and lead the way. He would then tempt the visitor to remain, invariably by offering candy. When he wished a door opened, he would place the hand of the one with him on the doorknob because of stiffness of his own right arm. He often asked what was wrong with him and why he could not speak distinctly, wanted to know if he would get well and appreciated that his blood pressure was elevated.

Although the general trend of this presentation has been optimistic, psychiatrists, like other physicians, have to face disagreeable facts. Organic deterioration, if more dynamic factors (new growths, infections or traumas) do not intervene, will eventually effect the demise of all of us. But thought must be given to those whose lives we prolong. We must strive to keep them as efficient as possible. The first case discussed here, which showed the beneficial result of a new job after retirement, recalls the words of Beckman.[21]

> We physicians must make it known that the aging and the aged we are keeping alive are not wrecks, incapable of carrying at least a part of the burden of their support. We must devise industries in which older persons work, else children will fling their parents to the State, and to be old will be horrible. We must convince political leaders that without the *productive* existence of the elderly, their vaunted economic security is no more than a shibboleth. We doctors must do this.

SUMMARY

Although the senile psychoses seem to be decreasing, the psychoses with cerebral arteriosclerosis are increasing so markedly that the psychoses of old age as a whole are showing a definite rise and are becoming the leading problem in psychiatry. Although the etiology of cerebral arteriosclerosis is still obscure, heredity and the tensions arising from environmental stress contribute an influence. There is a frequent lack of correlation between the severity of the mental symptoms and the extent of the cerebral damage. It is important to study these aging patients as persons who break down because of two sets of factors — personality problems and degeneration of brain tissues. The former may be reversible conditions, the successful treatment of which will modify the more static influence of the latter.

In a clinical approach we must distinguish between psychotic and nonpsychotic patients and also between senile and arteriosclerotic patients. In general, the greater the functional element present, the better the prognosis. The symptoms should not be studied or treated as distinct clinical entities but should be properly grouped into syndromes, and attention should be given to the timing of their onset as well as to the rapidity and evolution of their development. Often the variations in the blood supply to the brains of cerebral-arteriosclerotic patients leaves them intermittently psychotic. Their lucid moments should be capitalized on when questions of competency or the necessity of carrying out some business transaction arises. Their lack of judgment when psychotic makes them often dangerous to themselves, to others and sometimes to property, but it also leaves them vulnerable to the unscrupulousness of others.

When delirious or disturbing to others, they are best treated in a mental hospital in a quiet environment in which they can be more effectively handled without undue drug sedation or medication. The essential therapy consists of proper fluid and nutritional intake, proper elimination and a careful balancing of rest and exercise. When nonpsychotic and not too severely physically handicapped they should be kept busy. The greatest obstacle in effecting this is a sense of fatigue and lack of interest. Many patients may recover some degree of functional efficiency and return to their homes. Detailed observations in cases of questionable diagnosis are necessary. Many are more alert than might appear on superficial observation, are aware that they are inadequate and preserve some degree of intellectual integrity. Knowledge of these facts will not only prolong their lives but will make them more comfortable and give the physician the satisfaction of knowing that he has restored some of them to a productive status in their community. Physicians should use their influence to persuade legislatures, industrialists and those with more individual interests that this is possible.

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CARCINOMA OF THE CERVIX*

Survival in 98 Cases Treated with Five-Day Radium Only

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FOR over thirty years carcinoma of the uterine cervix has been treated with radium and x-ray used separately or in combination. Although various other procedures have been utilized, such as fulguration of small tumors, local excision or cervicectomy, radium has remained the standard method of treatment, giving the most reliable and consistent results.

In the past decade the use of radical surgery for the treatment of this carcinoma has seen a strong revival. Bonney[1] and Read[2] in England and Meigs,[3,4] Carter and Brunschwig in this country have championed the radical Wertheim operation. In their hands the morbidity of this procedure has been reduced to such a point that it may be considered on a par with the more widely employed radium and roentgen therapy. Recently reported results in large groups treated solely by radical operation are comparable in both mortality and morbidity to those achieved with radiation. Brunschwig[5] has reported the use of ultraradical surgery consisting of partial or total removal of the pelvic viscera for advanced cervical cancer.

The writing of this article was prompted by an unusual opportunity to study 98 cases of primary carcinoma of the cervix treated with five days' use of interstitial radium only. It is not our intention to imply that this is the preferred method of treatment. Furthermore, no attempt will here be made to evaluate various methods of radium application currently used for this tumor. The results herewith presented demonstrate what has been accomplished by the use of one treatment plan over a ten-year period by two surgeons, Drs. Leland and Swan.

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MATERIAL

From 1931 to September, 1943, Dr. George H. Leland, Jr., treated 262 women with carcinoma of the cervix at the Palmer Memorial Hospital. Throughout this period he employed radium in the form of radon gas in steel jackets, gold seeds or platinum needles containing 1, 2 and 3 mg. of the element. Roentgen therapy was used only as a palliative measure.

It has been the impression of several physicians concerned with the direction of the Palmer Memorial Hospital's Gynecological Outpatient Clinic that an unusually large number of patients treated with heavy doses of radium survived the five-year post-treatment interval. In an effort to establish a statistical basis for this impression a study of the radium-treatment records, morbidity and mortality of this group was undertaken. A cursory examination of the entire group (262 patients) revealed a variety of radium dosages varying from 3000 to 9000 milligram hours as the initial treatment. Further study revealed that at least 98 women with carcinoma proved by biopsy received a minimum of 6000 milligram hours, usually over a five-day period. It was also apparent that the last woman of the group had been treated at least five years prior to this study, thus furnishing the opportunity for a near-100-per-cent follow-up and five-year evaluation. An analysis of these 98 patients forms the basis of this report. Each patient was treated with primary dosages ranging from 6000 to

9000 milligram hours of radium only. In over 60 per cent the total dose was 7200 milligram hours (Table 1).

Method of Treatment

The standard plan of radium application used in this group consisted of the insertion of platinum needles into the cervical growth. The platinum needles containing 1, 2 and 3 mg. of radium were 1.65 mm. in diameter and 0.5 mm. in thickness; they were 60, 44 or 27.7 mm. in length. No central applicator was used. Under anesthesia the needles were inserted circumferentially, the 3-mg. strength usually in the center of the growth and the 1- and 2-mg. needles on the periphery of the lesion. The needles were allowed to remain five days *in situ* when the so-called long-term method was used. In some cases the total dose was given in four days.

No secondary dose of radium was used except for palliation or in cases of local recurrence. As mentioned, x-ray was not used as a part of the original treatment plan but only in treating widespread pelvic disease or focal metastases. Of the 98 patients, 24 received palliative roentgen therapy.

Table 1. *Analysis of Gross Radium Dosage Used.*

No. of Cases	Amount
	mg. hr.
19	6000
14	7000
60	7200
7	8000 to 9000

Classification

Clinical estimation of the lesion as seen at the first pelvic examination was based on the classification of the American College of Surgeons. When survival results were compiled this classification was converted to the new International classification. It is apparent that in transcribing Classes IB and IC to Stages II and III respectively there is considerable overlapping. For example, an advanced or late Class IB case might well be included in the Stage III group. In cases in which there was doubt (or an alternative listing as Stage II-III (1B–1C) was given), the earlier stage was chosen. This practice of favoring the earliest stage possible tends to lower the survival rate in each stage. An additional source of error in the initial recording of the stage of disease was the difficulty in judging broad-ligament involvement and the presence of pelvic-wall fixation. Several cases originally listed as Class 1A or 1B after only one to two months' observation revealed sufficient broad-ligament extension and lateral fixation to have been more properly grouped primarily as Stage III cases. In those cases that subsequently revealed advanced disease the first impression as gathered from the records was not changed. This practice also contributes to lowering the survival rate per stage. Morris and Meigs[6] state that in performing radical operations for cancer of the cervix they have found 18 per cent of Stage I cases to show positive nodes. This illustrates the error inherent in evaluating Stage I and II cases as such when the deep pelvic nodes are not palpable. Thus it appears that there may be a rather constant difference of opinion in the initial description of the tumor even on the part of experienced examiners. The comparative value of survival figures in the literature must necessarily be considered as relative, in that they concern individual interpretations of a three-dimensional lesion.

Table 2. *Analysis of Cases by Grade of Lesions.*

Grade	No. of Cases
II	15
II	27
III	40
Insufficient for grading	4
Unclassified	3
Adenoacanthoma of cervix	4
Adenocarcinoma of endocervix	1
Carcinoma simplex	4

Table 3. *General Complications.*

Complication	No. of Cases
Recurrent or unrelieved pain	17
Severe pelvic radiation reaction	5
Peritonitis and death (bowel perforation)	2
Phlebitis	2
Proctitis	2
Intestinal obstruction	2
Chronic leg edema	4
Rectovaginal fistula	4
Vesicovaginal fistula	1
Pyometria	1
Pelvic or retroperitoneal hematoma	3
Post-radiation fibrosis, fixation and thickening in pelvis	18

As may be seen from Table 5, the majority (75 per cent) of patients in this series had lesions described as either Stage II or III. There was no apparent correlation in the history with the duration of symptoms and extent of growth. Several patients with Stage III lesions gave only a two- to three-week history of brownish vaginal discharge prior to admission. Others with six months' symptoms might have an early or far advanced lesion.

The pathological criteria for grading of carcinoma of the cervix used at the Palmer Memorial Hospital were those previously outlined by Dr. Shields Warren.[7, 8] Briefly, this practice makes use of three rather than four histologic grades, as in the Broder classification. The three grades of differentiation are based on the degree of differentiation of the neoplastic cells. In this series there were 82 squamous carcinomas, the remainder falling into the

miscellaneous or undifferentiated group of lesions (Table 2). No significant correlation could be determined between histologic grade of tumor and period of survival.

Complications

Many gynecologists and radiologists concerned with the treatment of cervical disease believe that the average dose of 7200 milligram hours as used in these cases is too large for the routine treatment of Stage I and II lesions. Meigs[6] states that with a dosage of 10,000 milligram hours or more, using interstitial radium, one can anticipate a prohibitive morbidity. The opinion is often given that with the use of these amounts of radiation early lesions will tend to be overtreated, causing subsequent unnecessary complications and excessive damage to normal tissues.

We believe that a brief review of general and urologic complications as they occurred in this carefully selected group is pertinent to an evaluation of the slow-dose radium treatment. Several of these women suffered more than one complication, however (in tabulating these data the complications are listed separately — Table 3). In several cases it was impossible to decide whether or not the treatment or the disease itself was responsible for the pelvic complication.

Table 4. *Urinary-Tract Complications.*

Complication	No. of Cases
Hydronephrosis	2
Unilateral ureteral obstruction	3
Bilateral ureteral obstruction	2
Cystitis (radiation)	4
Incontinence	1
Pyelonephritis	1
Uremia	5

Eighteen of these women suffered with recurrent or unrelieved pelvic pain. Such pain is generally found in advanced lesions when the tumor has invaded adjacent organ-nerve areas and has produced marked fixation of tissues against the lateral pelvic wall. Failure in relief of pain is a discouraging factor in the use of radium for palliative or curative purposes. It may be remarked that in the extensive pelvic cancers thus far submitted to radical surgery a striking feature of the postoperative period has been the immediate relief of this disabling pain.

The manner in which both normal and neoplastic tissue will respond to a given dose of radium has been an unknown factor in radiation therapy since its inception. It is a common clinical observation that a rather small amount of radium may produce a marked tissue reaction in one patient and not in another. There may be a generalized pelvic radiation reaction, with associated cystitis and proctitis, or the production of vesicovaginal or rectovaginal fistulas. In this group a severe pelvic radiation reaction occurred in 5 patients. Such a reaction led to a rectovaginal fistula in 4 patients and a vesicovaginal fistula in one case. Several miscellaneous complications were found, such as pyometrium in one patient and pelvic or retroperitoneal hematomas in three women. Two patients died of radiation ileitis with perforation and peritonitis. Intestinal obstruction required laparotomy in two patients. It may be recalled that during the period in which these women were treated (1931–1943) no chemotherapy was employed.

As indicated previously, the degree of post-radiation reaction, with subsequent fibrosis, fixation and thickening in paracervical and parametrial tissue, that a given patient will develop is entirely unpredictable. Seventeen patients were seen at follow-up examinations to have considerable post-radiation fibrosis and thickening in the broad ligament, either unilaterally or bilaterally. This pelvic fixation was not necessarily productive of symptoms.

From the diagnostic standpoint it is always difficult in such cases, — even for the experienced observer, — to determine whether this fixation and thickening is simply radiation reaction or residual or recurrent disease. Usually time and frequent pelvic examinations with smears and biopsies will reveal its nature. Several investigators have pointed out that the vaginal smear may herald a visible or palpable recurrence several months in advance. We believe that a routine vaginal smear is very important in the post-treatment course of cervical cancer.

Delayed radiation reaction occurred in 2 patients and was of such unusual nature that it merits description. The first woman developed an ulceration on the lateral wall of the vagina three years after initial radiation. Despite the characteristics of recurrent disease, repeated biopsies from the advancing margin of the ulcer failed to demonstrate anything but necrosis and radiation reaction. The second woman, thirty-five years of age, developed an extensive ulceration at the vaginal apex five years after primary treatment of 7200 milligram hours. In this case also, repeated deep wedge biopsies failed to demonstrate recurrent carcinoma.

We have no immediate explanation for these cases, other than to suggest that some intercurrent infection or unnoticed trauma had caused a breakdown in this devitalized tissue.

Because of the intimate association of the lower urinary tract with the female reproductive tract, post-radiation complications are not infrequent. The incidence of complications in both the upper and lower urinary tract is shown in Table 4.

Survival

The five-year survival rate as related to the stage of disease is shown in Table 5. In this group of 98 women with carcinoma of the cervix, treated in-

itially for a five-day period with a minimum of 6000 milligram hours of radium, 47 women, or roughly half, survived five years. No cases of carcinoma *in situ* were included in the Stage I cases. The failure to achieve a near 100-per-cent five-year survival in lesions apparently confined to the cervix reflects in part the inadequacy of present-day treatment. It also appears from the results of operated cases that a 15 to 20 per cent error may be inherent in clinical estimation of Stage I tumors.

Although it is usually not difficult to recognize the presence of cervical carcinoma extending to the vagina, the presence and degree of broad-ligament involvement add uncertainty to the interpretation of Stage II growths. The relatively high survival rate (50 per cent) found in Stage II cases suggests that the majority may have been so-called "early" rather than "late" Stage II growths. A similar criticism might be directed at the high survival rate of Stage III cases, which is striking (44.7 per cent) as compared to that reported in the literature (8.3 to 23 per cent).

These women were only those reported to be clinically free of disease on follow-up evaluation. In the indeterminate group, 3 patients were lost to follow-up and were considered dead. Nine women died of intercurrent disease within the five-year period. The corrected over-all survival rate, excluding the deaths not due to cancer, then becomes 51 per cent.

The degree of health and comfort that the surviving patients enjoyed during these five years is not known. Fifteen of the women who survived five years were alive after a ten-year period. These patients are living and well and according to convention may be considered cured of their disease — although the probable fallacy of this assumption is well known, as a patient "cured" ten years may die of her disease at any interval thereafter. Twenty-two patients failed to survive the first post-radiation year. Of those dying at various intervals during the post-radiation period, 37 patients had evidence of metastases at autopsy. No patient with a Stage IV lesion survived more than two years.

Comment

Five-year survival results with combined radium and roentgen therapy for carcinoma of the cervix, as estimated from current literature, vary from 20 to 53 per cent.

Bowing,[10] in a report of 1631 traced cases from the Mayo Clinic, gives an over-all five-year cure rate of 32.8 per cent. The chief treatment in this group consisted of intensive broken-dose radium. In the latter part of the series roentgen therapy was used to supplement the radium.

A comparable large series is that of Munnell and Brunschwig[11] from the Memorial Center for Cancer in New York. In 1037 patients radiologically (x-ray and radium) treated, — including all four stages, — the five-year relative cure rate was 28.6 per cent.

A similar number of cases is reported by Morris and Meigs,[6] consisting of 1764 patients of all stages treated with x-ray alone, radium or radon and combinations of radium and x-ray but with no surgical procedure. Their percentage of five-year cures for 1764 patients was 20.3 per cent.

Waterman,[12, 13] in surveying end results over a fourteen-year period at the Rhode Island Hospital, cites an over-all five-year survival of 33.3 per cent in 579 cases. This group is comparable to the group of 98 patients discussed herewith, as the principle of small sources of radium widely distributed through the parametrium and paracervical tissues with heavy infiltration and long-time interval was used in both series.

It is obvious that the best results of radium treatment are noted in lesions of Stage I and II, those confined to the cervix and immediate adjacent tissues. Treatment failures in the more advanced cases, whether due to radiation resistance or to unsuspected extension of disease, suggest that alternate or supplementary methods such as x-ray or radical surgery must be used.

Table 5. *Five-Year Survivals in 98 Women with Irradiated Cancer.*

Stages	No. of Patients Irradiated	No. Surviving	Percentage of Patients Surviving
I	19	12	63
II	36	18	50
III	38	17	44.7
IV	5	0	0
Totals	98	47	47

As indicated previously, it is not the purpose of this report to advocate interstitial radium for the treatment of all cervical carcinomas. The plan herein presented was designed primarily for the management of Stage I and II growths. In the treatment of Stage III and IV neoplasms this method was used in some cases with the full knowledge that it was only a palliative measure.

This study represents a small series, and from the standpoint of a survival evaluation for cancer it may not be statistically valid. We do not consider this series in any way comparable to the end-results reported from larger clinics.

Summary

Survival rates are presented in 98 cases of carcinoma of the cervix treated only with an average dose of 7200 milligram hours of interstitial radium for a five-day period. Supplemental roentgen therapy was not used as part of the primary planned treatment.

These cases were treated during the period of 1931 to 1943 at the Palmer Memorial Hospital by the late Dr. George A. Leland, Jr. The results found in this analysis, giving an over-all corrected five-year survival rate of 51 per cent, are a tribute to the teachings and practice of Dr. Leland.

The authors are indebted to Miss Mary Kelly for the follow-up studies and to the nurses of the Palmer Memorial Hospital Outpatient Department for their unfailing co-operation.

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MEDITERRANEAN ANEMIA (HEREDITARY LEPTOCYTOSIS) IN A CHINESE FAMILY*

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BOSTON

HEREDITARY leptocytosis (Mediterranean anemia) is a disease seldom described in the Chinese race. Most of the cases reported in this group have been of the severe form of the disease, that is, Cooley's anemia.[1-5] That milder forms of this condition exist is now well established, but microcytic erythrocytosis with a high percentage of target cells in the peripheral blood, marked poikilocytosis, basophilic stippling and increased resistance of the red cells to hypotonic saline solutions. Features of the severe form of Mediterranean anemia, including erythroblastosis, splenomegaly, bone

TABLE 1. *Laboratory Data on Mild Mediterranean Anemia in Family M.*

PATIENT	AGE	SEX	RED-CELL COUNT	HEMOGLOBIN	HEMATOCRIT	MEAN CORPUSCULAR VOLUME	MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION
			millions	*gm.*	*vol. %*	*cu. microns*	*%*
H. M.	52	M	5.86	12.5	42	71.6	29.7
H. M.	50	F	4.73	14.1			
M. M.	32	F	4.09	12.5	41	100	30.4
M. M.	26	F	5.8	15.1	49	84.4	30.8
W. M.	24	M	5.18	9.5			
L. M.	22	F	5.54	12.5	41	74	30.4
F. M.	21	M	4.86	13.3			
A. M.	19	M	6.91	13.3	47	66	28.3
E. M.	16	M	5.85	11.3			
H. M.	14	M	7.04	12.9	51	72.4	25.2
L. M.	13	F	5.62	10.1			

unanimity of terminology concerning these cases is lacking. It is our purpose to report studies on a Chinese family, of which several members exhibited the typical hematologic findings of one of the mild forms of Mediterranean anemia, namely, hypochromic erythrocytosis.

Present Study

During the course of a diagnostic survey a young Chinese man was found to have a hypochromic changes by x-ray and evidence of a hemolytic process were lacking.

A study of the patient's family, including all 11 members, was made. They were apparently of pure Chinese ancestry and showed the characteristic Mongolian features of the Chinese. Table 1 summarizes the laboratory data; Figure 1 is a genetic chart of the family. The osmotic-fragility measurements were determined by the hemolytic-increment method of Suess and his co-workers[6]; serum-bilirubin determinations were made according to the method of Malloy and Evelyn.[7]

Seven of 11 members of the family exhibited the typical hematologic findings commonly seen in one of the mild forms (hypochromic erythrocytosis)

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of Mediterranean anemia. All the affected persons showed hypochromia, microcytosis, erythrocytosis, 8 to 25 per cent target cells in the peripheral smear, marked variation in the shape of the erythrocytes, basophilic stippling and increased hypotonic resistance of the red blood cells. Four members showed no hematologic abnormalities; all were in good health and were completely asymptomatic. None gave any history suggesting past hemolytic disease; none showed clinical jaundice or splenomegaly.

Discussion

Hereditary leptocytosis, or Mediterranean anemia, is an inherited disorder probably due to a disturbed hemoglobin synthesis resulting in various abnormalities of the red cell and in hypochromic anemia or hypochromic erythrocytosis.[8] Its incidence is greatest in the Italian, Greek, Syrian and Portuguese (that is, Mediterranean) groups, but cases have been described in almost all racial types except the Scandinavian. Dameshek[9] has described the several variants of the disease and has distinguished among severe, moderately severe and mild types. Genetic studies have been made by several observers, including Neel and Valentine.[10] The milder forms of the disease are transmitted as a Mendelian dominant from either parent. If two heterozygous persons marry, 25 per cent of their offspring will have the severe form of the disease, 50 per cent expectedly will show the mild form and 25 per cent expectedly will be unaffected.

Study of this Chinese family supports the reported genetic concepts. The father showed the mild form of the disease and was therefore presumably heterozygous. Siblings of the father were unavailable for study. The mother was unaffected. Six of their children were heterozygous, — that is, they showed the mild form of Mediterranean anemia, — whereas three children were normal.

Mediterranean anemia is a confining term and may be misleading. The term "hereditary leptocytosis," indicating a hereditary disorder in which thin target cells are found, is probably a better one and has recently received semiofficial sanction.[11] The present report emphasizes further that this condition exists in non-Mediterranean groups and even in the Orient. Chatterjea[12] states that cases are not infrequently found in India. Recognition of the benign form is important chiefly from the standpoints of prognosis and management; otherwise it has no particular significance, except with regard to heredity. Although the anemia is hypochromic, it is in no way benefited by orally or parenterally administered iron therapy, which is often given for long periods in these cases.

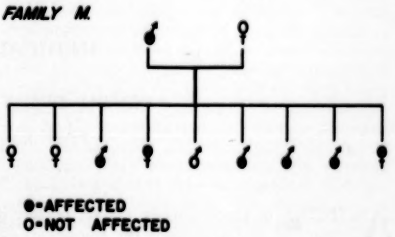

Figure 1.

Table 1 (*Concluded*).

Patient	Reticulocytes	Target Cells	White-Cell Count	Platelets	Osmotic Fragility	Serum Bilirubin
	%	%	/cu. mm.	/cu. mm.		mg./100 cc.
H. M.	0.2	12	8,800	402,560	I. R.*	0.5
H. M.	0.2	0	6,400	416,240	N.†	
M. M.	0.5	0	5,100	500 000	N.	
M. M.	0.6	0	8,500	460,240	N.	0.8
W. M.	0.6	12	6,750	400 000	I. R.	0.5
L. M.	0.3	12.6	4,300	409 600	I. R.	
F. M.	0.1	0	10 000	340 000	N.	
A. M.	0.1	25.2	10,600	1,980,000	I. R.	0.8
E. M.	1.4	18.6	4,800	431,450	I. R.	
H. M.	0.6	8.0	4,700	807,800	I. R.	0.5
L. M.	0.4	11.4	4,950	488,940	I. R.	

*Increased resistance.
†Normal.

Summary

A family of Chinese exhibiting a mild, asymptomatic form of hereditary leptocytosis (Mediterranean anemia) is reported. The genetic implications are reviewed and the importance of recognizing this disease in non-Mediterranean groups is emphasized.

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MEDICAL PROGRESS

DENTAL DECAY AND ITS CONTROL

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AN INDEX of the enormous public interest in control of dental caries is the amount of advertising carried by most American magazines on substances set forth as preventing or controlling tooth decay. Physicians as well as dentists are plagued with requests concerning such products; hence it is occasionally timely to review those phases of present-day knowledge pertinent to the instruction of patients.

Historically dental disease is as old as the record of mankind. There is some evidence that its prevalence is greater in modern than in ancient times. Conjecture is great but facts are meager about the effects on teeth of modern living habits. With the exception of the role of diet, little can be said concerning the causes of dental decay in primitive as against modern man.

Epidemiologically the disease has a world-wide distribution but varies geographically in incidence and intensity. Much conjecture has been made about the relation of caries to total sunshine, leaching of minerals from tilled soils, chemicals in water supplies, sources and marketing of food and racial influences, but the factual evidence to support any particular theory is slight. An exception is the study of Dean and his co-workers demonstrating differences in the incidence of dental caries between communities having measurable amounts of fluorine salts in the water supply and communities in which these salts were absent. There is no doubt that the presence of these salts in natural water supplies is one constant factor that appreciably reduces the expected incidence of tooth decay in these areas. However, much more is involved in the problem of prevention than the addition of fluorine to drinking water.

Clinically, caries may be characterized as progressive destruction of the specialized cells composing the coronal portion of the dental structure after they have been expelled from their developmental crypts into the local environment of the oral cavity. Susceptibility or immunity varies widely. Occasionally the lesion is initiated in the cementum covering the root of the tooth.

The sequelae of tooth decay, — infection, loss of teeth and so forth, — will not be discussed in this report.

Initiation of the carious lesion invariably takes place on the exposed surface of the tooth. The order of vulnerability of the tooth surface to attack is the inverse of their order of exposure to mouth function. Thus the order of vulnerability is: deep anatomical pits and fissures in either normal or abnormal teeth, surfaces in contact with adjacent teeth, recesses not contacted by adjacent mouth structures (the tongue, lips and cheeks) and surfaces not utilized in mastication — for example, the tooth area at the marginal gingivae.

Disintegration is achieved by disorganization or decalcification of the inorganic substance. Decomposition or necrosis of the organic substance of the tooth is an accompanying process. Decalcification is most likely achieved by an acid potential with a pH of about 5.0 retained in local contact with the tooth enamel. This frequently accompanies plaque formation on the tooth surface. The plaque is a mucous mass of low solubility richly imbedded with acid-producing organisms and closely adherent to the tooth. Acid production is most plausibly explained as the action in the mouth by microbial enzymes on a suitable substrate of high carbohydrate content. This theory has pointed the way to many avenues of productive investigation both in vivo and in vitro.

A few investigators minimize the acid theory of tooth disintegration. They favor the theory of proteolytic breakdown along the interprismatic substance of the enamel and believe control rests in an "impregnation" technic of silver salts. This theory, of which Gottlieb is the chief proponent, has not met with favor among the majority of investigators of dental decay. Although it has not been completely refuted, enough evidence has

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not been offered to make further pursuit along these lines attractive.

Genetic factors may operate in the production of caries, for, as any observant dentist knows, there is a striking similarity of susceptibility or immunity in children and parents. Whether this similarity is the result of like environment or due to inherent constitutional factors is not entirely clear. The correspondence is particularly striking when both parents are markedly caries-free or caries-susceptible. Few dependable data are available, however, to support genetic theory. Klein, studying the effects of fluorides on individual teeth, concluded that part of the immunity was dependent on inherited factors. Compelling interest in genetic factors is the fact that experimental laboratories have developed certain strains of animals that are regularly immune or regularly susceptible through successive generations, though exposed to the same environment.

Nutrition unquestionably has an important constitutional influence on the incidence of dental caries. Although Sognnaes concludes that "the developmental influence does not seem to be determined specifically by any one single nutrient among those currently recognized as being essential to general health, growth and reproduction," he does agree with Mellanby that "structure of developing teeth can be significantly altered by changes in the calcifying properties of the diet." It is the writer's belief that much must yet be done to determine specifically the "calcifying properties" of the diet when related to the physiology of the teeth.

Many investigators have reported, both clinically and in the laboratory, instances of the addition or removal of specific dietary components that seem to alter the course of dental disease. Whether these factors alter the host or agents that produce decay is frequently disputed. It is difficult to separate for clinical use the words "diet" and "nutrition."

Although milk is an important and relatively cheap source of the mineral components important to the structure of developing dental tissues, there is ample evidence that sound teeth may be present in the mouths of people when this article of diet is scarce or lacking but the necessary mineral constituents have been made available through some other dietary sources. On the other hand, developing teeth may be rendered less vulnerable to subsequent decay by the fluoridation of drinking water, but there is no evidence that fluorides are a physiologic necessity or that the human organism is incapable of developing sound teeth in their absence. Indeed, the presence of these salts in proportions much greater than two parts per million of total fluid intake is known to be toxic to a number of body tissues.

Two facts of interest to the general practitioner about nutrition and sound teeth seem important. First, those foods supporting general health and growth according to present-day standards of pediatric care are probably adequate for dental development without fortification by special foods or prescribed drugs. This does not mean that the teeth may not benefit if the attending physician prescribes dietary supplements for a patient in need of them, but for caries alone vitamin prescriptions are not indicated. Nor does this mean that the child living in an area in which fluorides are available in the water supply may not have a reduced susceptibility to dental decay. Up to the time of this writing no satisfactory *safe* prescription has been reported for this chemical that may be dispensed with the same reliability as vitamins. No prescription for mineral support to the normal diet has been proved effective for protection against dental decay. Secondly, the coronal portion of the teeth, which is that part vulnerable to decay and which is largely formed by the age of twelve, has no known exchange mechanism for its mineral content. Thus, just as the work by Albright and others indicates that the physiologic withdrawal of minerals from the tooth is impossible, it seems improbable that continued mineralization can occur after the tooth has erupted into service. Evidence against this last statement has not been adequately supported.

The influence of disturbed nutrition or disease on physiologic development of the teeth, even when insufficient to produce a recognized syndrome, is to be found in a more distinct record in the dentin or enamel than in other tissues, in which cellular change and recovery are more labile. Identifiable diseases, — endocrinopathies and congenital defects, — invariably influence the developing teeth sufficiently to render their condition a part of the diagnostic syndrome, and thus, by the alteration of structure, influence susceptibility. Although many diseases may alter the supporting and adjacent structures, the influence of fully developed teeth, except as the condition alters the oral environment, is negligible. Thus, further discussion of the effect of systemic illness is beyond the scope of this report. Although the structure of teeth is unquestionably modified by physiologic disturbances, it is difficult to determine whether any specific episode acts as the primary factor to determine caries susceptibility. It is difficult, if not impossible, to measure all the other factors known to contribute to dental disease. For example, the literature on the relation of emotional disturbance to dental caries is increasing, yet the writer finds it difficult to separate the direct effect of neurologic disease on the involved dental tissues from that of possible change in oral hygiene. Perhaps the difficulty is a matter of semantics.

Bacteriologically, no single organism seems to be specifically pathognomonic of the disease, al-

though the constancy of varying strains of lactobacilli tends to put these organisms in that category. A number of acid-producing organisms are capable of surviving and multiplying in media sufficiently acid to etch teeth in situ. Jay, Becks and others make use of the constancy of lactobacilli to measure personal susceptibility to dental caries by culturing organisms from the mouth on a suitable medium and counting the colonies. When the carbohydrate in the diet is altered, — thus influencing the substrate, — they report that the number of colonies will decrease and the amount of decay will lessen.

Studies on the metabolism of oral micro-organisms associated with mouth physiology, plaque formation, acid production and subsequent decay of teeth are abundant and promise a clearer understanding of the sequence of events in the future. More information and a better understanding of the multiple factors involved may lead to effective control methods. In particular, we can hope for some explanation of the differences between caries-free and caries-susceptible persons who, seemingly, have a similar heredity and environment. It must be borne in mind that the teeth are outside the body — a reasonable explanation for the fact that attempts to create an antibody reaction against the organisms associated with decay have been essentially fruitless.

Hygiene and diet are almost as difficult to separate in this discussion of the multiple factors involved in the production of caries as are nutrition and diet. Hygiene is a paramount environmental influence on teeth. The collection of plaques and materia alba in the mouth has a direct relation to the conditions of eating and hygiene. An unclean mouth may well be the result of lazy or inefficient oral action, such as is found in mild myopathy or malocclusion. On the other hand, a pappy diet, consisting of adhesive foods with no "detergent" foods, may be a contributing cause of poor dental hygiene in an otherwise healthy mouth.

Reliable reports have appeared on the reduction of caries in children surviving near-starvation diets in regions affected by war. Some reporters attribute this to the alteration of oral biosis. If the children are underfed, perhaps the organisms associated with dental decay starve. Other investigators attribute the lowered incidence of decay to the lowered intake of carbohydrates, particularly in the form of refined sugars. Both groups may be partially correct, but unquestionably either premise carries an important implication for our overfed (with respect to carbohydrates) American children. Although complete hygiene is impossible to achieve, it is probably true that "a clean tooth never decays."

It seems clear that cleanliness will at least assist in removing the microbial plaques and that caries control is therefore improved. Tooth brushing and mouth cleansing are important and should be encouraged by the physician. The method of brushing, type of brush and choice of dentifrice are perhaps best decided on by the family dentist at the first visit — some time after the second birthday. The accumulation of food débris in the mouth is conducive to progressive increase of lesions in caries-susceptible persons. For this reason the teeth should be brushed and the mouth rinsed frequently, preferably after eating and always before retiring.

Diet, from a physiologic standpoint, is determined by nutritional demands and, as stated before, needs no special supplements for caries control per se. There is ample evidence that the careless use of carbohydrates in even a nutritionally adequate diet may be cariogenic. As previously mentioned, mouth hygiene is important for the removal of excessive carbohydrate substrate, but dietary supervision is also important for the caries-susceptible patient. All fermentable sugars and starches should be kept at the minimum for such patients, but particular effort should be made to free the diet of refined sugars as used on cereal, in desserts and so forth. Candy and sweet beverages, especially as used for between-meal snacks, should be forbidden. This is the only known dependable dietary control of the disease.

Dental service is still the preferred method for control of the carious cavity. Since decay is a progressive process, the thorough excavation of the small cavity and its prosthetic replacement is the best known check for the existing lesion.

Fluoridation in certain urban areas of controlled community water supply to a concentration no greater than one part per million has now been in effect for a sufficiently long period to affect the developing dentition of young children. The reduction of expected dental decay has been as great as 30 per cent. This satisfying result should not be allowed to go unquestioned, however. Although no clinical reports have been published from these areas of the effects on other body tissues, the physical and laboratory examinations of selected groups or epidemiologic studies of the vital statistics of the entire populations have not been exhaustive or prolonged enough to guarantee the method as without danger. It must be remembered that the greatest benefit is received between birth and the age of twelve years. Whether or not certain members of the population, such as those suffering from chronic illnesses, are affected by concentrations of this magnitude is unknown. The writer would like to go on record as not vigorously opposing the method but as regretting that the authorities responsible for existing experiments have not pursued such investigations more exhaustively.

Topical fluoridation, for rural areas where controlled water supply is not available, by the use of weak solutions of sodium fluoride on cleansed dried teeth *in situ* has been suggested. Experiments show some promise for this method when carefully exe-

cuted by a dentist or a specially trained technician. Whether or not this procedure is economical for mass prophylaxis is still to be determined. The reported results of experiments are so varied that the writer has not been persuaded to enthusiasm for this method. Furthermore, long-range studies may indicate the necessity of continued application throughout life, once the procedure is initiated, for maximum protection; there is some evidence that treated mouths may show a slight increase in caries susceptibility when applications are discontinued. The exact mechanism of protection is not clear. In the writer's opinion, until more information is available the method should not be recommended without reservation and should be reserved for patients in whom a known high caries index has been established early in life. It is possible that even weak solutions of 1 per cent or less may have a deleterious effect if applied to exposed dentin; therefore all existing cavities should be filled before treatments are given.

Fluoride compounds in pills, lozenges, dentrifrices and so forth are not recommended. It should be remembered that fluoride compounds are extremely toxic and even lethal in reasonably small doses. Self-medication of any sort should be strictly avoided.

The production of dentifrices containing penicillin is still in the experimental stage. Only two experiments have been published by reliable investigations, and the results are completely opposed. In the writer's opinion, the use of antibiotics in dentrifices shows no more promise than the transiently appearing antiseptic preparations offered in the past.

Chlorophyll-impregnated dentifrices have not been sufficiently tested to justify the claims made for them by their manufacturers.

Ammoniated dentrifices, though theoretically valuable, as evidenced by reduction of Lactobacillus counts, has not been significantly useful in the practical reduction of new carious lesions. At present it is doubtful that this product will cause sufficient caries reduction to sustain its present widespread popularity.

A comprehensive bibliography relating to all the facts and suggestions incorporated in this report would be too voluminous to be practical. The reader is therefore referred to Easlick's book,* which largely covers the modern concepts of dental caries and contains an extensive bibliography.

300 Longwood Avenue

*Easlick, K. A. *Dental Caries*. 234 pp. St. Louis: C. V. Mosby Company, 1948.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

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CASE 37441

PRESENTATION OF CASE

First admission. A fifty-six-year-old man was admitted to the hospital because of headaches and heart trouble.

About nine months before admission the patient was told that he had high blood pressure (200 systolic), but he felt well at the time. Four months prior to entry he began to notice easy fatigability. He slept fairly well but at times awakened in the morning with severe headaches; these usually disappeared before breakfast but at times lasted all day. Two months before admission he became ill with generalized aching, feverishness, perspiration, anorexia and diarrhea 5 to 6 times daily, preceded by lower-abdominal cramps. This lasted approximately two weeks. Since that time he had felt more tired and noticed slight exertional dyspnea and swelling of the ankles. Ten days before admission, after playing 36 holes of golf, he first noted paroxysmal nocturnal dyspnea. Treatment with digitalis and restriction of activity resulted in disappearance of the paroxysmal nocturnal dyspnea and increased strength and well-being. There was no history of angina, cough, orthopnea or renal disease.

There had been recent nocturia 2 to 4 times nightly with a little hesitancy and a poor trajectory. There had been a twenty-pound weight loss over a five-month period.

On physical examination a few wheezes were heard over the apex of the right lung and at the base of the left lung. The heart was enlarged to 1.5 cm. beyond the midclavicular line in the fifth intercostal space. There were rare premature beats and a Grade II apical systolic and faint Grade I aortic systolic murmur. The aortic second sound was greater than the pulmonic. The abdomen was normal. On rectal examination the prostate was twice the normal size. There was + edema of the ankles. All peripheral pulses were palpable and normal except the right dorsalis-pedis pulse, which was somewhat diminished.

The pulse was 80 and the respirations 20. The blood pressure was 200 systolic, 125 diastolic.

Urinalysis showed a specific gravity of 1.020, a + albumin and rare hyaline and granular casts in the sediment. Examination of the blood revealed a hemoglobin of 12.8 gm. and a white-cell count of 9700, with a normal differential. The nonprotein nitrogen was 41 mg. and the fasting blood sugar 89 mg. per 100 cc.; the serum sodium was 138.5 milliequiv., the potassium 4.7 milliequiv. and the chloride 104 milliequiv. per liter. One stool gave a ++ guaiac test, but 3 subsequent tests were guaiac negative. An electrocardiogram showed a normal rhythm at a rate of 90, a PR interval of 0.18 second, small notched P waves, a tendency to left-axis deviation, and one ventricular premature beat; the ST segment was depressed in Leads 1, AVL, V_3 and V_6; the T waves were diphasic in Leads 1, AVL, V_3 and V_6, upright in Leads 2, 3, AVF, V_1, V_2 and V_5 and inverted in Lead V_4. Comparison with a tracing made five months before admission showed essentially no change except for slightly less inversion of the T waves on the left side. A phenolsulfonphthalein test showed less than 5 per cent excretion of the dye after 15 minutes and about 25 per cent excretion in two hours. Two urine-concentration tests showed specific gravities of 1.020.

An x-ray film of the chest and fluoroscopy showed no pulmonary disease. The costophrenic angles were obliterated and there was a suggestion of a small amount of fluid in each pleural space. The heart was enlarged in the region of the left ventricle, where pulsations seemed diminished in amplitude. The hilar vessels were slightly increased in prominence. X-ray films of the skull demonstrated some osteoporosis of the posterior clinoid process and an unusually prominent vascular groove in the left frontal region. A barium-enema examination was negative and a gastrointestinal series was negative except for some delay in passage of barium through the lower esophagus where it crossed the tortuous aorta.

The patient felt well until the fourth hospital day, when he suddenly became confused, did not know where he was, did not recognize his physician and talked confusedly about his business. About two hours later he was again mentally clear and oriented and realized that he had been confused. No neurologic abnormality could be demonstrated at this time except sluggish reflexes in the knees and ankles. He subsequently remained mentally clear, with no further episodes of this type. He was discharged on the eighth hospital day on digitoxin, 0.1 mg. twice a day, and a low-sodium diet. At the time of discharge he felt well subjectively, the chest was completely clear and the pulse was regular at a rate of 76.

Second admission (eight days later). For the first two days at home he was able to climb one flight of stairs daily. Then he became gradually weaker. Two days before entry he began to have dull, intermittent, then constant, burning nonradiating pain in the right upper quadrant that became gradually worse. There was no nausea, chills, fever, jaundice or dark urine. The stools were allegedly slightly lighter than usual. The pain was only partially relieved by 50 mg. of demerol orally and recurred subsequently.

On physical examination the heart was enlarged as on the previous admission, but in addition an apical systolic gallop was present. A few rales were heard in the left chest. There was tenderness and spasm in the right upper quadrant of the abdomen. The liver was percussed 3 to 4 cm. below the costal margin but was not palpable.

The temperature was 98°F., the pulse 80 and the respirations 22. The blood pressure was 210 systolic, 150 diastolic.

Urinalysis showed a specific gravity of 1.021, a ++ albumin, and a few red cells, white cells, hyaline casts and granular casts in the sediment. A urine urobilinogen was 1.0 Ehrlich units in a two-hour specimen. The white-cell count was 17,850, with 86 per cent neutrophils, and the hemoglobin 12 gm. The serum bilirubin was less than 0.2 mg. direct and 0.3 mg. total, the serum total protein was 6.73 gm. with an albumin-globulin ratio of 2.1, the nonprotein nitrogen 72 mg. and the amylase 47 units per 100 cc.; the sodium was 134.9 milliequiv., the chloride 98 milliequiv. and the potassium 4.4 milliequiv. per liter. The cephalin-flocculation test was ++ after forty-eight hours. Five stools, one of which was tarry black, were guaiac negative. A Graham test showing fairly good concentration of the dye was negative. A plain film of the abdomen demonstrated gas throughout the colon and in several loops of small bowel, none of which appeared definitely distended.

The abdominal pain persisted and nausea and vomiting developed, but the patient remained afebrile, with a pulse rate between 90 and 100. The white-cell count on the fourth day was 29,200 with 93 per cent neutrophils, on the fifth day 16,400 and on the eleventh day 33,600. On the sixteenth day duodenal drainage showed clear, dark bile with abnormal amounts of calcium bilirubinate and a rare white cell in the sediment but no cholesterol crystals. A Graham test at this time showed no contrast substance in the gall bladder and a few days later another test showed very faint filling. There was no evidence of stones.

The abdominal pain persisted, requiring narcotics for relief. The patient had no appetite and continued to vomit. The white-cell count remained elevated and the nonprotein nitrogen fluctuated between 40 and 60 mg. per 100 cc. The serum electrolytes showed no significant change. Four whole-blood transfusions were given. On the twenty-eighth day an operation was performed.

Differential Diagnosis

Dr. Alfred Kranes*: This story divides itself conveniently into two admissions that appear to be independent of each other, although there was an interval of only eight days between them. The first admission appears to have been the result of straightforward hypertensive heart disease with left-ventricular failure, as evidenced by the paroxysmal nocturnal dyspnea, although on admission to the hospital he showed no signs of congestive failure. As one reads the entire history and reflects a bit about the first admission, nagging doubts about whether this actually was uncomplicated hypertension begin to arise. There are a number of strange features about it. In the first place, reading between the lines without actually having seen the patient, I get an impression that he was somewhat sicker than might be expected with uncomplicated hypertension. There had been easy fatigue and a two-week illness with fever, diarrhea and abdominal pain — which perhaps may have been acute gastroenteritis that lasted longer than one ordinarily expects such an episode to last. Also there had been a 20-pound weight loss. This may have been occasioned by the fact that he was told to take off some weight because of high blood pressure. If so, the weight loss was not significant. As the story unfolded, it did not resemble the course of uncomplicated hypertension. Within a period of nine months he developed renal failure and cardiac failure. He had an episode of what I presume to be hypertensive encephalopathy during the first admission. Patients with hypertension do not develop cerebral, cardiac and renal manifestations within a period of nine months unless they have malignant hypertension. I do not see how I can make a diagnosis of malignant hypertension unless he had involvement of the fundi. No mention was made of an examination of the fundi. Were they normal?

Dr. Chester M. Jones: Essentially normal.

Dr. Kranes: With normal fundi I cannot make a diagnosis of malignant hypertension — yet the course suggests it. It certainly does not suggest ordinary hypertension. I shall leave that question in abeyance for the time being and go on to the second admission, which is the one that concerns me.

It appears from the record that during the eight days that elapsed between admissions something took place in the abdomen that caused a good deal of pain, nausea, vomiting and the striking leukocytosis without fever. If any questions are raised by the first admission, the second is even more puzzling. It is at least comforting to know that those who took care of this patient were likewise puzzled. The three Graham tests and the duodenal drainage are ample evidence of this.

Were there other examinations of the abdomen during the second admission, Dr. Jones? I am given only the initial examination, during which spasm and tenderness were elicited in the right upper quadrant. Were they constant or did they vary a great deal?

Dr. Jones: They varied, but during a three-week period he had right-upper-quadrant spasm and rebound tenderness almost all the time. There were days when the abdomen was softer and no rebound tenderness was present, but it was present more frequently than it was absent.

Dr. Kranes: It puzzles and disturbs me that four blood transfusions were given before he was operated on, and the only hemoglobin reported was 12 gm. I deduce that during his hospital stay the hemoglobin must have dropped considerably.

Dr. Jones: It dropped to a low of 9.7 gm., and there were black stools on one or two occasions.

Dr. Kranes: Guaiac positive?

Dr. Jones: The one that was reported as being black had a guaiac-negative reaction.

Dr. Kranes: I find that somewhat difficult to interpret.

Dr. Jones: We all did.

Dr. Kranes: I should be concerned about giving 2000 cc. of whole blood to a man who had recently had paroxysmal nocturnal dyspnea, but it probably was given slowly and the physicians got away with it all right.

May I see the x-ray films now?

Dr. Joseph Hanelin: There is no change in the appearance of the chest in the six-month interval before operation. The heart is enlarged, with the left ventricle predominantly affected. The lungs are emphysematous. I do not believe the pulmonary vessels are particularly prominent. The blunting of the costophrenic angles appears to be due to thickened pleura rather than to fluid. There is scarring in the region of the left lower lobe, which appears to be both fibrous and calcific, with a suggestion of pleural calcification in the major septum. The skull films are not contributory. There is nothing to suggest increased intracranial pressure.

Dr. Kranes: During the second admission was a gastrointestinal series repeated?

Dr. Hanelin: No; it was not. The stomach, duodenum, jejunum and colon appear normal.

Dr. Kranes: Is the duodenum normal? One disease to be considered is a perforated duodenal ulcer.

Dr. Hanelin: It looks normal. At the first examination the gall bladder is satisfactorily visualized. Two and a half weeks later there is non-visualization of the gall bladder by the Graham test and only faint concentration of Priodax within it when the test was repeated two days afterward.

Dr. Kranes: Are we sure that the tablets were not vomited at the second and third examinations?

Dr. Jones: I do not know; I saw this patient a good many times during the course of events, but I do not recall that.

*Associate physician, Massachusetts General Hospital.

DR. KRANES: It must be considered, but the nurses usually call it to the attention of the physician if a patient vomits the tablets.

DR. HANELIN: A slight amount of calcification is seen in the wall of the abdominal aorta — but nothing to suggest an aneurysm; the film of the abdomen was made several weeks before operation and gives no real further clue to the trouble.

DR. KRANES: There was no striking enlargement of the liver.

DR. HANELIN: No; it is not a huge liver.

DR. KRANES: One wonders whether the symptoms of the second admission could have been in any way related to the first. Was this all due to congestive heart failure and a large, tender liver? Some enlargement of the liver between the two admissions was implied but was never definitely stated. However, there were no good confirmatory signs or symptoms of congestive failure during the second admission. I do not see how congestive failure with a tender liver could explain the course during the month in the hospital, particularly the extraordinary leukocytosis and the development of anemia. He appears to have gone steadily downhill, so I do not see how I can offer that as a logical explanation.

Since the patient was known to have hypertension, could the pain have been due to a complication of hypertension? The only complications of hypertension are vascular in origin, — either thrombosis or hemorrhage, — and are customarily confined to the heart and cerebrum, but they may be found elsewhere. Could he have had, for example, a mesenteric thrombosis? There certainly was not much evidence of intestinal obstruction, even though he had been vomiting throughout the final illness. There was no distention of the small or large bowel. Certainly those who were taking care of him would not have allowed him to go untreated for twenty-eight days if they suspected intestinal obstruction. As for hemorrhage, — abdominal apoplexy, so-called in many of the older medical textbooks, — despite the tarry stool I do not see how I can seriously consider that.

Perhaps he had some independent disease having no relation to the hypertension. Certainly the x-ray and clinical findings suggest some localized disease in the right upper quadrant — specifically the gall bladder. I think one must conclude that he did have some disease of the gall bladder. But once one makes that statement it is about as far as he, — at least I, — can go. It certainly was not a stone; a stone would not explain the whole picture, and I doubt that he had a stone despite one duodenal drainage that showed an increased amount of calcium bilirubinate. Acute cholecystitis is possible, but the constant pain, nausea, vomiting and high leukocytosis without any fever are against such a diagnosis. One thinks of more serious involvement of the gall bladder, such as empyema or gangrene; if so, I would expect the duodenal drainage to have yielded more than an occasional white cell, and I would expect more fever. The same objections pertain to the various suppurative, inflammatory and even neoplastic diseases of the gall bladder. He had a fairly well filled gall bladder on the first examination, and it is difficult to believe it was the site of, for example, carcinoma.

What about the liver? There was no good evidence of liver disease. The ++ cephalin flocculation is within the normal range, and both the clinical and laboratory examinations lend no support to the possibility that he had intrinsic liver disease. Hepatoma? I suppose it is a possibility. I have seen several cases of hepatoma with extreme leukocytosis.

Another consideration is a slow perforation of a duodenal ulcer with a subhepatic abscess. The gastrointestinal series was negative on the first admission, and it seems improbable that he had an ulcer that perforated, or an acute ulcer between the two admissions; in either case one would expect some fever.

What about acute or subacute pancreatitis? I do not think one can dismiss that quite so readily. The patient had an elevated serum amylase; he had constant pain, although it was not where one normally expects pancreatic pain to be; and he had constant nausea and vomiting — all somewhat suggestive of acute or subacute inflammatory pancreatic disease. For those reasons I do not believe that one can disregard that possibility.

However, none of these possibilities satisfy me completely. When one is not satisfied, he begins to wander into the realm of generalized diseases that have local manifestations that may mimic other diseases. Outstanding examples of these are lymphoma and polyarteritis. I do not see how we can take lymphoma very seriously, for there is no evidence on which to make such a diagnosis. However, I cannot dismiss polyarteritis quite so readily. It certainly would explain a great deal that seems obscure in this picture. It would explain the questions I raised about the first admission — the rapid progression of the hypertensive disease in the absence of any fundal changes and the fact that he seemed to be much sicker than ordinary hypertension would warrant. Would it explain the extreme leukocytosis with a normal temperature? The abdominal pain of polyarteritis is not likely to be as constant, severe and prolonged as this, — it is usually recurrent, — but I would not say that it ruled it out. One disturbing feature about such a diagnosis is that according to the record something apparently happened in the eight days between admissions that caused a great deal of pain and resulted in a very high white count. Furthermore, one wonders whether the abdominal disease had anything to do with what had occurred before.

The rule of this game requires that one make a diagnosis. The diagnosis that one makes in this case,

it seems to me, depends on whether he thinks this man had one or two diseases. If one thinks he had two diseases, he has to make a diagnosis of hypertension, with its complications, and in addition some intra-abdominal disease — most likely subacute pancreatitis. If one thinks the patient had one disease, then I cannot see any way of escaping the diagnosis of polyarteritis nodosa. After due consideration, I think this patient did have one disease — and that it was polyarteritis nodosa.

DR. JONES: I think one statement that Dr. Kranes made should be modified. I think he said the serum amylase was elevated. It was actually normal. It was only 47 units. I do not believe one has a right to call that elevated.

I saw this patient with Dr. Daniel Ellis on several occasions. At no time were we convinced that he had disease in the gall bladder, although we had thought of it very seriously. Two weeks before he was operated on I thought he had a certain amount of congestive failure secondary to hypertensive disease and that the abdominal pain was probably on the basis of arterial thrombosis in the abdomen. I think that Dr. Ellis also thought vascular disease in the abdomen was the probable basis of the pain. The picture was not at all clear. The most striking things were the constancy of the pain, the relative constancy of the abdominal findings of tenderness and more or less spasm and the very high white-cell count, running as high as 33,000 without much elevation of temperature — 99.5°F., on the average. We believed the symptoms and signs that he had were more consistent with a vascular accident and vascular disease than with any other condition. He was explored because we believed an operation had to be done to make a diagnosis.

DR. MAURICE FREMONT-SMITH: What sort of vascular disease did you call it, Dr. Jones? Did he have an infarction?

DR. JONES: Because it happened very suddenly shortly before the second admission, we were inclined to think he had a thrombosis of a branch of one of the large arteries of the abdomen.

DR. EARLE M. CHAPMAN: Of the liver, Dr. Jones?

DR. JONES: No; because the liver was felt and was not tender.

DR. CHAPMAN: Would thrombosis of the cystic artery produce that?

DR. JONES: I think it could.

DR. CHAPMAN: The high white-cell count also brings that to mind — the lack of fever and the high white-cell count.

DR. WALTER BAUER: I agree with Dr. Kranes' diagnosis. Very frequently patients with polyarteritis nodosa have a leukocytosis of the degree reported with slight or no fever. I too believe the sequence of events and the rapidity with which they took place are all consistent with a diagnosis of polyarteritis nodosa.

DR. KRANES: Don't you think it was a strange hypertension?

DR. BAUER: Yes; it progressed rapidly, as it can in polyarteritis nodosa.

DR. BENJAMIN CASTLEMAN: Have you any comment, Dr. Aub?

DR. JOSEPH C. AUB: I am glad somebody else was discussing this case! I notice that Dr. Kranes did not pay any attention to the red cells in the urine.

DR. KRANES: If the diagnosis is correct, it would explain the urinary findings.

CLINICAL DIAGNOSIS

?Carcinoma of the body of pancreas.
?Arterial thrombosis in abdomen.

DR. KRANES' DIAGNOSIS

Polyarteritis nodosa.

ANATOMICAL DIAGNOSIS

Polyarteritis nodosa.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Before operation, as Dr. Jones stated, there was quite a difference of opinion about what this man had, and it varied from day to day. One day it was chronic cholecystitis. When Dr. Leland McKittrick saw him, he said: "If this is not a cardiovascular disease I suspect carcinoma, probably primary in the body of the pancreas." Dr. Ellis's last note ended with the diagnosis of malignant disease and of course that is one reason that the patient was operated on — although he did say: "The white count is more in line with an infectious process." Dr. McKittrick's preoperative diagnosis was question of carcinoma of the body of the pancreas.

At operation he found a lesion in the midportion of the pancreas that measured about 5 by 6 cm. in diameter. He called me to the operating room at the time. Although the surface of the pancreas looked perfectly normal, he thought he would try to get a biopsy; he could not reach what he believed was a small mass in the pancreas. The biopsy looked to me like normal pancreas. The gall bladder was slightly reddened, with many venous thrombi in its wall; there were no stones. The right gastric artery was almost completely occluded and was markedly calcified. He was unable to feel any pulsation in it, although he felt good pulsation of the celiac axis. He took a biopsy of the gall bladder and of the right gastric artery also. The postoperative diagnosis was pancreatitis or carcinoma of the body of the pancreas. Microscopically the biopsy of the pancreas showed many small arterioles with very severe intimal hyalinization, such as one may see in a patient with hypertension. We found thrombosed veins in the wall of the gall bladder and also some thrombosed arteries consistent with the severe

arteriosclerosis. We believed that all the symptoms could probably be accounted for by the severe sclerosis of the abdominal vessels — something to which Dr. John Sproull often says we do not pay enough attention. He said some years ago, in discussing a clinicopathological case, that we pay attention to coronary sclerosis, cerebral sclerosis and peripheral-vessel sclerosis but rarely pay attention to the branches of the abdominal arteries, which may become sclerotic and may cause symptoms. That is what some physicians have described as abdominal angina. That is what I thought this patient had.

Soon after operation the patient developed increasing uremia; he became oliguric and then anuric, and the nonprotein nitrogen went up to about 150 mg. He died with a severe bronchopneumonia five days postoperatively.

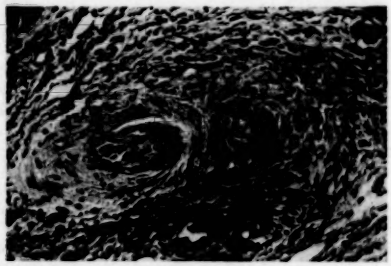

FIGURE 1.

At the time of autopsy we sectioned the head of the pancreas and found a large hematoma, most of which I believe was recent, perhaps as a result of the biopsy that Dr. McKittrick took — but that was only part of it, as the edge of the hematoma showed real organization, indicating that part of it had been present for some time. The microscopical section showed an organized thrombosis of a good-sized artery close to the hematoma. We also found at autopsy complete thrombosis of the right gastric artery and thrombosis of the cholecystic artery, a branch of the hepatic. The hepatic artery, although sclerosed, was quite patent, as was the celiac axis itself.

I scheduled this case for a clinicopathological conference with the idea in mind that it was an example of abdominal angina due to arteriosclerosis and severe hypertension. Last night I looked at the autopsy slides for the first time and was amazed to find just what Dr. Kranes predicted. The wall of the gall bladder showed an old thrombosis with necrosis of the arterial wall and a cellular infiltration around it; the mucosa was perfectly normal. This morning I had deeper sections cut of the biopsies of the gall bladder and pancreas and did find more vessels with complete thrombosis and recanalization and some with acute necrosis and granuloma in the wall of the vessels (Fig. 1). The kidneys showed, in addition to arterial disease, focal areas of necrosis in the glomeruli — findings that we have now begun to see quite often in patients with polyarteritis nodosa. There were so many casts in the tubules (and in places an extruded cast with a cellular reaction) that I wondered whether there was a slight lower-nephron nephrosis as well. If he had received sulfonamides eight or nine months previously when he had the infection, an allergic reaction to the drug might explain the pathogenesis of the polyarteritis. Whether the hypertension was cause or effect in this case is not clear; there has been a recent report suggesting that hypertension may be a factor in the etiology.*

*Kipkie, G. F., and Johnson, D. S. Possible pathogenic mechanisms responsible for human periarteritis nodosa. *Arch. Path.* 51:387-392, 1951.

CASE 37442

PRESENTATION OF CASE

A forty-seven-year-old man was admitted to the hospital in an unresponsive and incoherent condition.

One week prior to admission he began to complain of general malaise. On the following day he developed a severe cough productive of large amounts of rusty sputum and subsequently began to vomit ingested food. Shortly after this he had a number of shaking chills and began to feel very warm, as though he had a "fever." He remained coherent and active, although the cough, fever and vomiting were unchanged. Three days prior to admission it was noted that he was less responsive and that he used his right arm and leg with considerable difficulty. He became incontinent of urine and feces. A diagnosis of lobar pneumonia was made and he was started on intramuscularly administered penicillin. Shortly thereafter the coughing and vomiting subsided. However, the patient became progressively more drowsy, and twelve hours before admission he became totally unresponsive. It was noted that his respirations were rapid and accompanied by many crackles and bubbles.

For many years the patient had "bronchial trouble," with a mild cough. One year prior to entry he had bronchopneumonia with an apparently uneventful recovery. For many years he had consumed large quantities of alcohol daily.

Physical examination revealed a sallow, semicomatose man propped up on pillows, with rapid bubbling respirations. The neck veins were flat. The heart was negative. There were coarse inspira-

tory and expiratory rales and rhonchi throughout both lung fields but no definite dullness. There was moderate clubbing of the fingers. There was no edema or cyanosis. He responded to painful stimuli only on the left side. The eyes were roving, and he seemed unable to see to the right. The pupils did not react. There was right-facial weakness and flaccid paralysis of the right arm and leg. The patellar, Achilles and radial reflexes were equal and active. The triceps and biceps reflexes were slightly more active on the left. Plantar reflexes were flexor.

The rectal temperature was 103.6°F., the pulse 120 and the respirations 40. The blood pressure was 150 systolic, 90 diastolic.

Urinalysis was negative except for a + albumin. A urine culture and smear were negative. Examination of the blood showed a white-cell count of 14,800, with 84 per cent neutrophils and a hemoglobin of 12 gm. A sputum smear revealed gram-positive cocci and gram-negative cocci, diplococci and rods. A throat culture showed abundant growth of alpha-hemolytic streptococci and moderate growth of catarrhalis. On lumbar puncture the initial pressure of the spinal fluid was equivalent to 220 mm. of water and the final pressure equivalent to 160 mm. of water. The fluid was cloudy yellow, and contained 7500 white cells per cubic mm., with 92 per cent neutrophils. The total protein was 1040 mg. per 100 cc., the chloride 102 milliequiv. per liter and the sugar 37 mg. per 100 cc. The colloidal gold curve was 5555555555 and the spinal-fluid Hinton test negative. Cultures of the spinal fluid grew *Staphylococcus albus* and *B. subtilis*. An x-ray film of the chest showed a clear right lung field and considerable density in the left upper lobe and probably in the lower lobe as well. A round shadow approximately 4 by 3 cm. was present at the level of the hilus. The heart was not enlarged.

The patient was started on streptomycin, penicillin and digitalis. Examination on the second day showed the following additional findings. The neck was stiff; there was pain on movement and a positive Kernig sign. The pupils now reacted to light. Eye movement to the left was normal, but to the right there was not only impairment of gaze but there was also a lack of conjugate movement, with the adducting eye not moving as far to the right as the abducting eye. The right plantar reflex was extensor and the left flexor. On lumbar puncture the spinal fluid was under a pressure equivalent to 230 mm. of water and contained 3500 white cells per cubic mm. The total protein of the fluid was 220 mg. per 100 cc., the chloride 118 milliequiv. per liter and the sugar 41 mg. per 100 cc. Culture of the fluid showed no growth. On the third day the spinal fluid was turbid and contained 1900 white cells per cubic mm., with 90 per cent neutrophils. By the sixth day the spinal fluid was clear and subsequently never contained more than 150 white cells per cubic mm. Physical findings remained unchanged, with the temperature ranging from 100 to 103°F. On the eleventh day the temperature rose to 105°F., the coma deepened and the patient died quietly.

Differential Diagnosis

Dr. Maurice Fremont-Smith*: A history of a patient admitted in stupor and whose family cannot be present is always unsatisfactory. Had this man had any sinus or ear infection? Had any headache preceded this condition? Because he had clubbed fingers, I should like to know how much cough he had and whether he had sputum.

Dr. Benjamin Castleman: Dr. Adams, can you answer any of those questions?

Dr. Raymond D. Adams: No.

Dr. Fremont-Smith: The urinalysis was negative except for a + albumin. I should like to know if there were any red cells.

Dr. Castleman: The urine did not contain red cells.

Dr. Fremont-Smith: The sputum smear was nonspecific. The throat culture showed alpha-hemolytic streptococcus, which is so common in the throat that it may mean nothing. The picture of the spinal fluid is interesting; it definitely shows a very severe bacterial meningitis. The chloride and sugar were low, both going with bacterial meningitis. The colloidal gold curve could have been of any type with the amount of protein that was present in that fluid. The cultures grew *Staphlococcus albus*, and there is no question about the fact that he had meningitis.

There was a statement that the heart was negative. I dislike statements like that. I should like to know more about the heart. The patient was given streptomycin, penicillin and digitalis. The neck veins were not engorged and the physicians thought he had no heart failure. Why digitalis? The second neurologic examination is the one that I think was the more careful one. The neck was stiff, with a positive Kernig sign. The eye movements to the left were normal, but to the right there was loss of conjugate deviation. Also on the right side there was paralysis of face, arm and leg and a positive Babinski sign, showing that he had some serious intracranial lesion on the left. The conjugate movement of the eyes would be affected by a lesion somewhat anterior to the motor area. It is obvious that both the left motor and left sensory areas were involved, as he had lack of sensation on the same side as the paralysis. Hence, he must have had a severe lesion in the left cortex in addition to the meningitis. The interesting thing is that as the man grew worse and died the spinal fluid became better and cleared.

May I see the x-ray films?

Dr. James J. McCort: The x-ray films of the chest are not very helpful. They were taken with

*Associate physician, Massachusetts General Hospital.

portable apparatus on a semicomatose patient lying in bed, and only anteroposterior films could be obtained. The right lung is clear and there is no fluid in the right pleural cavity. On the left side there is a hazy increase in density in the left upper lobe and the lobe is reduced in size, particularly in the region of the inferior and superior lingular segments. Adjacent to the hilum and in the region of the left-upper-lobe bronchus and the lingular bronchus there is an irregular soft-tissue density. A small amount of fluid is seen in the left pleural cavity. Both leaves of the diaphragm are in their normal position. No gross abnormality of the heart and vessels is seen.

DR. FREMONT-SMITH: The things we know about this man are that he had a bacterial meningitis, an intracranial lesion and a condition that was called a pneumonia; it may have been pneumonia and may have cleared under the antibiotics. Apparently the antibiotics also cleared the spinal fluid. It seems to me that a collection of pus in the region of the left cortex or below the left cortex has to be considered as the focal point of the meningitis, and the question is: Where did this pus arise from? It is very like a lesion below the diaphragm — a subdiaphragmatic abscess or a liver abscess that causes sterile fluid or even at times a slightly infected fluid above the diaphragm. I think the patient had something within the brain that broke through, causing meningitis, but that the meningitis was a secondary affair.

What could be the source of an infected bacterial lesion in the substance of the brain? Well, it may have been an embolic phenomenon. Subacute bacterial endocarditis, I think, rarely causes an actual abscess in the brain. An acute endocarditis with metastases might cause an abscess in the brain. That is one possibility, but there are a great many things against it. The heart was said to be negative. Almost always there is a loud systolic murmur with acute endocarditis. There was no evidence of embolic phenomena elsewhere in the body — the urine contained no red cells; the spleen was not said to be enlarged; there were no petechiae in the fingers or conjunctivas. As none of these were present, I think endocarditis is probably to be ruled out.

Another condition, — a very interesting one, — is subdural empyema — a condition described by Kubik and Adams[1] in 1943. Subdural empyema is a condition that is not usually recognized, but if it is recognized the patient can sometimes be cured, as were two of their patients. It usually arises as a result of severe infection in the paranasal sinuses or in the ear. Dr. Kubik and Dr. Adams reported 14 cases, 13 of which arose from the sinus or the ear. There was one case that was metastatic from bronchiectasis. The symptoms are headache, stiff neck, fever, confusion, later coma, very frequently paresis or paralysis of the opposite side, a conjugate deviation of the eyes, — inability to move the eyes to the paralyzed side, — and often convulsions. In none of these cases was there an actual bacterial meningitis. There were signs of meningismus, but the cultures were negative in all cases. In no case was the cell count as high as in this case. However, the condition does need to be considered, as one can let out the pus through a burr hole, sometimes saving the patient by this procedure. I refer you to Kubik and Adams' interesting report.

The other possibility, — and the one that I think is the most likely, — is that this man had a lesion in the chest, possibly bronchiectasis but more probably abscess. Bronchiectasis is usually bilateral, and it is often not visible in the plain x-ray films. I think he had a metastatic abscess from the lung to the brain, — either multiple or a single brain abscess, — and that such an abscess broke through the cortex and infected the meninges and that the patient therefore developed a bacterial meningitis.

DR. ALFRED KRANES: This man had clubbing of the fingers, so perhaps the chest lesion had been present for a long time. If it was, then perhaps it would be less likely to be an abscess than bronchiectasis with pneumonia — repeated pneumonias on top of the bronchiectasis.

DR. FREMONT-SMITH: I think that is a good point. Repeated pneumonias are more likely to be subsequent to bronchiectasis than to an abscess.

DR. THOMAS PAINE: There is one point about the bacteriologic studies: The spinal fluid grew out *Staphylococcus albus* and *B. subtilis*. I think the presence of *B. subtilis* raises a rather large question about the nature of the real infecting organism. I do not think one can believe that *Staphylococcus albus* was the real infecting organism here, since the other organism was present.

DR. FREMONT-SMITH: Isn't *B. subtilis* much more likely to be a contaminant?

DR. PAINE: Yes; therefore, I must suspect that the staphylococcus may also have been a contaminant.

DR. JOHN T. STANBURY: I wish the radiologist would consider the lesion in the hilum consistent with carcinoma in the lung. This might be an abscess secondary to carcinoma of the lung.

DR. MCCORT: I do not see how one can exclude the possibility of carcinoma of the left-upper-lobe bronchus on the basis of this limited x-ray examination.

DR. STANBURY: This man was an alcoholic. Such patients are quite prone to infection with Friedländer's bacillus; that can give rise to lung abscess. I wonder if that type of abscess metastasizes to the brain.

DR. CASTLEMAN: Any type of lung infection may metastasize to the brain.

DR. MCCORT: Was a cytologic examination of the sputum done?

DR. CASTLEMAN: I do not believe one was done.

DR. PAINE: What did the gram stains of the spinal fluid show?

A PHYSICIAN: We saw no organisms.

DR. FREMONT-SMITH: The fact that the chloride and sugar were lowered must mean that there were bacteria in the spinal fluid.

DR. JAMES B. AYER: If the time relations given here are correct, this man was well until only a week before admission. Therefore, I hardly think he had a subdural infection of the extent that is suggested, and I also think the sinuses would have shown some disease. The fact that he was well and then acutely ill suggests bacterial meningitis, perhaps with the infection more severe on one side than on the other, which is not uncommon. I have seen cases of *Staphylococcus albus* meningitis that ran a mild course without specific treatment. *B. subtilis* is a fairly common contaminant. A small abscess as an initial point of infection is possible, but I think that a thrombophlebitis is more so. Death would not necessarily be due to meningitis. I suspect that there was something else, such as a block of the cerebral fluid, perhaps from medullary pressure.

DR. CASTLEMAN: We have the two authors of the paper on subdural empyema right here. Dr. Kubik, have you any comment?

DR. CHARLES S. KUBIK: Of course, metastatic subdural empyema is a rare condition. The cell count in the fluid was rather high for that, as Dr. Fremont-Smith pointed out. The rapid course might suggest that possibility, but I should think that an intracerebral abscess would be more likely.

DR. ADAMS: We saw this patient on the ward. The arguments that the Medical Service used were something as follows: This man clearly had a meningitis because of all these cells in the spinal fluid and the low sugar. However, the lateralizing signs came on so early and were so prominent that it was obviously more than an ordinary bacterial meningitis. Usually lateralizing signs in bacterial meningitis develop rather late in the second or third week of the infection and are often due to thrombophlebitis. In this case they were the first indications of intracranial disease. We assumed, therefore, that the patient had an abscess in the brain that had ruptured into the ventricle, or a septic embolus that produced focal areas of destruction and a bacterial meningitis. Unfortunately, the history was not sufficiently complete to determine by the rate of onset which of these two conditions had occurred. There was no source of embolus. Abscess was thought most likely, but since the patient was moribund when seen the Neurosurgical Service thought he would not survive a brain operation.

CLINICAL DIAGNOSIS

Metastatic brain abscess.

DR. FREMONT-SMITH'S DIAGNOSES

Metastatic brain abscess from bronchiectasis of the lung, with rupture into meninges.

Meningitis.

ANATOMICAL DIAGNOSES

Brain abscess, left parietal lobe (bacteroides), metastatic from lung abscess.

Ventricular empyema.

Cerebellar pressure cone.

Cirrhosis of liver, alcoholic type.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed that the pulmonary lesion was in the inferior posterior portion of the left upper lobe. It proved to be a benign abscess that apparently had produced a metastatic abscess to the brain, which Dr. Adams will tell us about. There was a fairly severe alcoholic cirrhosis.

DR. ADAMS: From the time the brain was first exposed, on removal of the calvarium, it was clear that it was abnormal. The surfaces were flattened, and the left cerebral hemisphere was much broader than the right — especially its posterior half. Over the left parietal lobe the convolutions were unusually broad and flat. The arachnoidal membrane along the base of the brain and over the posterior aspect of the spinal cord was opaque and whitish, but no subarachnoid exudate could be seen on gross inspection. There was a sizable left-cerebral pressure cone, compressing the medulla. Coronal sections of the brain disclosed a large abscess occupying the left parietal lobe; it extended almost from the superior frontal region back to the occipital region and inferiorly to the temporal lobe. It was filled with pale-greenish exudate of fetid odor. When it was removed one could see that the wall of the abscess was thin, rather pinkish and evidently lacking in fibrous connective tissue. The abscess extended from the cerebral cortex to the ventricle into which it had ruptured. The abscess was in a position to produce a hemiplegia, homonymous hemianopia and aphasic disorder such as were observed in this patient. The rupture into the left lateral ventricle was obviously responsible for the meningitis. Death very likely was related to the ventricular empyema and the cerebellar pressure cone.

DR. KRANES: Was any organism cultured?

DR. CASTLEMAN: The bacteriologic aspects were of particular interest. The abscess of the lung showed a predominance of *Staphylococcus aureus*, as well as many other organisms. From the brain abscess we obtained a pure culture of bacteroides. I think this is very significant and may explain the lack of response to antibiotics. Apparently the bacteroides organisms are quite unresponsive to antibiotics. Dr. Ropes, you have been studying this.[2, 3] Would you agree?

DR. MARIAN ROPES: I agree; I think the evidence is still very poor concerning whether any chemotherapy or any of the antibiotics help. There are a few reported cases in which it seems possible they do. Because of the presence of *Staphylococcus albus* in some cultures it may have been assumed that it was the responsible organism. The bacteroides might not grow out for two weeks, and unless the cultures were kept a long while, — up to two weeks, — it might explain the absence of bacteroides in the spinal fluid.

DR. CASTLEMAN: The staphylococci may have overgrown the bacteroides that was there.

DR. PAINE: That is certainly a good suggestion. Bacteroides is a very strict anaerobe. It does not grow unless one incubates the culture under strictly anaerobic conditions for a long while.

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REPORT FROM STOCKHOLM

THE fifth General Assembly of the World Medical Association, — a meeting the significance of which was emphasized in these columns on August 16, — took place in Stockholm September 16 – September 21. The Council of the Association held its twelfth meeting September 9 – September 15 and convened for its thirteenth session on September 22, after the elections held by the Assembly, continuing its labors into the following day. September 21 was given over to the second annual meeting of medical editors, a convention that was inaugurated in New York in the fall of 1950, on the occasion of the fourth General Assembly.

The real and arduous work of the Association is accomplished by committees and in the Council sessions. The Assembly initiates, discusses and ratifies this work and provides that most ancient and most democratic of all proceedings — an open forum.

At the recent meeting, with the medical associations of over thirty countries represented, Dr. Elmer Henderson, in turning over the presidency to Dr. Dag Knutson of Sweden, reviewed the activities of the Association and Council during the past year, stressing particularly the close relations that have developed between the Association and the World Health Organization and other international bodies. In addition, he reviewed the objectives of the Association in medical education and the desire of the organization to sponsor a world conference on this important subject.

The delegates of three new member associations were welcomed, — those of Japan, Western Germany and Thailand, — and the associations of the Republic of Korea, Burma and Haiti were voted into membership. The Association's pledge of support to the World Health Organization was again affirmed.

Three sessions of the Assembly were given over to a discussion of social security as it affects medical practice, with the delegates of every country represented participating, as well as a number of observers. Of particular interest was the variance of the views expressed on this controversial subject. The majority, as is to be expected, were opposed to what is generally called socialized medicine, because of its political implications and the conditions under which physicians are expected to care for their patients.

Dissenting to greater or less degree from this prevalent opinion were the three Scandinavian countries, in which a moderate socialism has been in effect for some time. Dr. Johan Haffner of Norway particularly stressed the general satisfaction of Norwegian physicians with the circumstances under which they work and disagreed with the majority opinion that compulsory participation should apply only to those patients who cannot otherwise take care of their medical expenses. In Norway, he stated,

90 per cent of the population is covered by the present state-administered system.

As a result of this general expression of opinion on social security, the matter was referred to the Council for further study.

One came away from a meeting of this new world-wide association (still less than six years old) with a belief in the fundamental value to mankind of such an effort. This belief must be based not on any recorded concrete accomplishments at this early date but on the simple fact of the existence of the organization and the good will that it represents. It is further tangible evidence of the ceaseless struggle that man in his desire for the right is making against man with his proclivity for unrighteousness.

PROLONGATION OF LIFE FOR PHYSICIANS

THE mortality data of physicians was the subject of a study, several years ago, by Dublin and Spiegelman.[1] In the group fifty-five through sixty-four years of age an 11.2 per cent increase was shown in the annual death rate of physicians over that of the population in general, as compared with a study made in 1925.[2] In the same age group the ratio of the death rate of physicians to that of white men in general was 1.11 to 1.0. There were higher death rates for physicians from the degenerative conditions but much lower death rates from most infectious diseases and surgical conditions. These and other studies confirm the marked increase in the death rate of physicians over forty-five from arteriosclerotic and coronary disease as compared with the white male population. The increase in deaths from the leukemic disorders among radiologists as compared with non-radiologists[3] has also been pointed out as probably due to a specific environmental factor.

The possible etiologic factors and preventive measures have recently been discussed by Lewis.[4] His views on the matter of prevention should interest all physicians. He cites the well known carelessness of physicians in seeking medical attention early, their reluctance to take up the time of their busy colleagues and perhaps the failure of some physicians to give their fellow physicians the benefit of their most painstaking attention. Studies of executive personnel and the examination of physicians for admission to the armed services indicate the large number of abnormal findings in all adult groups. Thus an annual physical examination is one of the primary preventive measures for the physician to adopt, — as it is for the layman, — in order that the earliest abnormal changes may be detected. Many business firms are more advanced than medical societies in providing medical clinics for employees and in arranging for medical check-up on their executives. The thought is expressed by Lewis that some prepayment plan might be established or organization dues arranged to provide clinical facilities for examination and advice on treatment for physicians and perhaps for their families. Perhaps a state medical society, with the assistance of the Blue Shield or an insurance company and a few local hospitals in the state, could join forces to furnish such services to the members of a state medical society and their families. In the interests of really good preventive medicine such a service should begin early in the life of the physician. Such clinics might also have considerable influence in stimulating more laymen to seek annual medical examination. Pediatrics has already done much toward this end concerning the routine examination of children, and many adults profit by a regular check-up. Emphasis on the principles of mental and physical hygiene for physicians and laymen could be a further benefit of such a program. The principal benefit will be the prolongation of the life of many middle-aged physicians — men who have too often died in the full bloom of their valuable accumulated experience with patients and with disease.

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MEDICAL EDUCATION IN 1951

THE postwar confusion that swirled about medical care and medical education in the United States is subsiding. Although a good deal of smoke was generated (and is still apparent in some quarters),

1951 has witnessed a significant clearing of the atmosphere, with more light and less heat than in any recent year. The panic about doctor shortages has largely subsided, although the military uncertainties amid which the world exists haunt it with all kinds of narrow margins. Some of the earlier reports on the cost of medical education now appear to have been unduly pessimistic. Partial relief has been initiated by the medical profession itself and promises to be continued in the immediate future — yet in the opinion of many who are wrestling with the problem this help can only be a part of a multilateral program if the challenge to the retention of present standards of medical education is to be fully met.

The medical schools have, during the past academic year, enrolled the largest number of students in their history. This was revealed in the fifty-first annual report of the Council on Medical Education and Hospitals of the American Medical Association, a total of 26,191 students having enrolled in the 79 approved medical schools of the United States. Of these, 7182 were entered in the first-year classes. It is estimated that 7400 new students will embark this fall on the study of medicine in the schools of the nation. Privately owned schools enrolled 54.2 per cent of the total of medical students last year, which was slightly less than the percentage (54.9) of the previous year.

The schools graduated 6135 physicians last year, the largest number for any year except 1947, when with the termination of the wartime accelerated schedules several schools graduated more than one class of students. In the seven years before World War II the annual graduations from approved schools ranged from 5089 to 5377. In 1920 there were 2680 graduates. True, the population of the land is much greater, hence the relative number of physicians does not increase with this increased output. In 1920 there was one physician for every 729 persons; in 1950, one for every 730.

Although the relative numbers of physicians have not increased, there can be little doubt that their quality has greatly improved, that they render more services, that their services are more effective and that they are altogether a more substantial support of the nation's health than ever before. This is true partly because the educational processes are constantly improving and partly because of the selective process applied to candidates for admission to the schools.

Seventy schools were able to supply information on the scholastic records of those applicants accepted for admission. Approximately 40 per cent of the students entering medical school last year had "A" averages, another 40 per cent had "B" averages and almost 20 per cent had averages of "C" or lower in their college work. The survey of the previous year indicated that only 9.1 per cent of the entering students had "C" averages. The falsity of the irresponsible charge that students who do not maintain a straight "A" average in college have little or no chance of being admitted to medical school was thus pointed out. It is significant, however, that no students who had "D" averages were admitted.

FOCAL INFECTION AND SYSTEMIC DISEASE

THE June issue of the *Journal of the American Dental Association* is devoted to a report by Dr. Kenneth A. Easlick, professor of dentistry and of public-health dentistry at the School of Public Health of the University of Michigan. This report is entitled "An Evaluation of the Effect of Dental Foci of Infection on Health." It is based on a review of the literature and was prepared after consultation with a number of leading authorities in medicine and dentistry. It contains discussions of the mechanism of focal infections, of the various problems in the diagnosis of focal infections from nonvital or diseased vital teeth and of the role of such infections in diseases of the joints, heart, kidneys, eyes and skin.

The impetus for this review was obviously derived from the demonstration of the effects of cortisone and ACTH on rheumatoid arthritis and on many other diseases of unknown origin in which focal infections have, during the past quarter-century, been thought to play an important etiologic role. During this period, as pointed out in the editorial that accompanies this review, countless teeth have been removed in an effort to cure or relieve various systemic disorders. The scarcity of

instances of lasting improvement resulting from dental surgery in such cases has raised considerable doubts concerning the rationale of this procedure. The demonstration of the effects of the adrenal hormones in many of these disorders obviously calls for a new appraisal of the role of focal infections in such conditions.

The Magnetic Herald from Earlville, Madison County, N. Y., will never kill anyone by its shocks.

Boston M. & S. J., *November 5, 1851*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

Bartlett — Oliver L. Bartlett, M.D., of Lenox, died on October 8. He was in his ninety-second year.

Dr. Bartlett received his degree from Columbia University College of Physicians and Surgeons in 1887.

His widow, two sisters and a nephew survive.

Collins — Aubrey J. Collins, M.D., of Hyde Park, died on October 3. He was in his seventy-seventh year.

Dr. Collins received his degree from Tufts College Medical School in 1902. He was a fellow of the American Medical Association.

His widow survives.

Cort — Parker M. Cort, M.D., of Springfield, died on September 27. He was in his seventy-fourth year.

Dr. Cort graduated from Harvard Medical School in 1902. He was a member of the Clinical Club, the Springfield Academy of Medicine and the American Medical Directors Association.

His widow, a son and a daughter survive.

Germain — The death of Harry H. Germain, M.D., of Belleair, Florida, has been reported. He was in his seventy-seventh year.

Dr. Germain graduated from Harvard Medical School in 1898. He was a member of the American College of Surgeons and a fellow of the American Medical Association.

His widow and a daughter survive.

Withington — Alfreda B. Withington, M.D., of Pittsfield, died on October 2. She was in her ninety-second year.

Dr. Withington received her degree from the Woman's Medical College of the New York Infirmary for Women and Children in 1887. She was a former president of the Berkshire Medical Society.

No immediate relatives survive.

MISCELLANY

THE SELECTIVE SERVICE SYSTEM

The following information has been received from the National Advisory Committee to the Selective Service System.

Release from Service

The Department of the Navy is using the following policy in regard to release from service of physicians and dentists (former registrants and reservists):

Priority I	24 months
Priority II	12–24 months
Priority III	24 months
Priority IV	
(12 months during World War II)	12–17 months
(Less than 12 months during World War II)	12–24 months

The Department of the Army is operating, at present, on the following program:

Any physician or dentist who served 12 months during World War II becomes eligible for release after 17 months of current service, except those called in Organized Reserve Units, who will serve the full 24 months.

The Department of the Air Force is operating, at present, on the following program:

Any physician, dentist or veterinarian may request release after 21 months of service. If he was in Priority I or II, the 21 months must be during the present term of service.

Induction Group

Requests for delay in active-duty orders have been asked for some of those physicians who accepted commissions after receiving orders for induction and before being inducted. This is entirely out of order except where there are very special extenuating circumstances. Therefore, the Health Resources Advisory Committee is calling all records of such cases to Washington for review. In fairness to the State Committees, there have been instances where such delays have been requested and granted without the knowledge of the Committee or without regard to the advice of the Committee.

Physician Draft

The following item was taken from *Selective Service* for August, 1951:

The planned induction under Selective Service of 333 Priority I medical officers scheduled during the month of August has been delayed temporarily at the request of the Department of Defense.

In requesting the delay, the Department of Defense stated that the delay was based entirely upon an unanticipated and sustained increase in the number of doctors applying for Reserve Commissions in the Armed Forces. Whether or not all of the doctors, whose induction will be delayed during August, will be called during September is dependent upon the volunteer rate during the next few weeks, the Department of Defense said.

The Secretary of Defense has indicated that no reduction is anticipated, at this time, for the call of 152 Priority I doctors scheduled to be inducted during September.

Physician Inductions

The following item was taken from *Selective Service* for September, 1951:

State Directors have reported to National Headquarters that many of the special registrants ordered by their local boards to report for induction on the July call, for 717 doctors, were found to have been previously commissioned. This brought to light the fact that the Armed Forces were not in every instance forwarding a D. D. Form 44 to his local board after a man was commissioned.

Since the July call for special registrants was issued, the Armed Forces have commissioned 429 doctors. Of this number, 333 received Army commissions, 186 Air Force, 3 Navy, and 7 were commissioned by the United States Public Health Service.

Incomplete reports from the States also disclosed that 10 doctors were declared physically unfit; 80 were reclassified, postponed, or cancelled; 2 were inducted; an indefinite number are still pending for one reason or another; and another very small number are believed to be delinquent and will be reported as such by their local boards.

Of the two inducted, it has recently been reported in the public press that one of them agreed to accept a commission after completion of 3 days' service as an enlisted man.

CORRESPONDENCE

ANTITHYROID DRUGS AND ACUTE THYROIDITIS

To the Editor: In the September 6 issue of the *Journal*, Reveno and Rosenbaum present a report of three cases of acute thyroiditis in which it is suggested that the employment of antithyroid drugs effects a salutary influence on the course of the disease. There are two points that bear comment with regard to this conclusion.

The first is that the natural course of the disease is such as to make evaluation of antithyroid agents difficult. Since

1940, 11 cases of acute thyroiditis have been seen in the Thyroid Clinic of the Massachusetts General Hospital The courses have been sufficiently diverse to allow the interpretation that the cases described or cited by Reveno and Rosenbaum[1] merely exhibit variations in the natural course of acute thyroiditis, unaffected by the therapy employed.

The second is that the effects of acute thyroiditis on thyroid function and iodine metabolism are such that antithyroid agents should logically exert no influence on the process. Recent studies in this laboratory and in others[2,3] have shown that in severe acute thyroiditis profound abnormalities of the basal metabolic rate, serum protein-bound iodine and radio-iodine uptake are frequently encountered. Characteristically, the basal metabolic rate is somewhat elevated, the protein-bound iodine is moderately elevated and the radio-iodine uptake by the gland is markedly reduced, often to so-called myxedematous levels. It is interesting that the basal metabolic rate may, however, at times be normal despite a significant elevation of the protein-bound iodine.

The best explanation for this triad of normal or increased basal metabolic rate, increased protein-bound iodine and depressed radio-iodine uptake seems to be the following: The effect of the acute inflammatory process on the thyroid gland is twofold — to cause a discharge of existing iodinated thyroglobulin or iodinated amino acids, or both, into the blood stream and to suspend (generally temporarily) the ability of the thyroid gland to accumulate iodide ion from the circulation. This would explain the hyperthyroidism that may transiently accompany this disease and the hypothyroidism that may supervene late, in those glands that do not recover function. The occasional finding of an elevated protein-bound iodine in the absence of an elevated basal metabolic rate or of clinical hypermetabolism raises the question whether or not iodinated amino acids other than thyroxine, such as diiodotyrosine and monoiodotyrosine, which are of minimal calorigenic potency, may be released from the thyroid gland in this state. As yet no data are available on this subject.

To return to the possible effect of blocking agents on acute thyroiditis: The thiourea group of compounds inhibit organic incorporation of iodine but do not impair iodide collection by the thyroid gland. Since the thiourea drugs are reducing agents and since the trapped iodide must be oxidized to iodine before iodination can occur, it is thought that these compounds act to inhibit this oxidative step, either directly or by virtue of enzymatic inhibition. Since the gland in acute thyroiditis cannot accumulate iodide ion, a metabolic block is thus already present, at a stage of iodide metabolism preceding that at which thiourea would act — in effect the type of block that would be created by large doses of thiocyanate. Thus it is extremely unlikely that antithyroid agents could be effective in this process, unless these agents possess some hitherto unrecognized anti-inflammatory action. Furthermore, there is no evidence that antithyroid drugs affect the rate of release of preformed thyroxine, and it has been clearly shown that these agents do not impair the peripheral action of thyroxine, hence one would not anticipate any alleviation of thyrotoxic symptoms on such bases.

James B. Wyngaarden, M.D.
Thyroid Laboratory
Massachusetts General Hospital

References

1. King, B. T., and Rosellini, L. J. Treatment of acute thyroiditis with thiouracil. *J. A. M. A.* 129:267, 1945.
2. Robbins, J., and Trunnell, J. B. Effect of thyroid stimulating hormone in acute thyroiditis. *Tr. A. Goiter A.* (in press).
3. McConahey, W. M. Radioiodine studies in thyroiditis. *Tr. A. Goiter A.* (in press).

BACK NUMBERS OF *JOURNAL* NEEDED

To the Editor: The University Library, Scientific and Medical Department (49, Nörre Allé, Copenhagen N, Denmark) has tried in vain to procure back numbers of the *New England Journal of Medicine*.

We need especially Volumes 175-224, 226 and 229.

It is our hope that the readers of the *Journal* may be able and willing to help us. We will, of course, gladly pay all transport expenses, and can offer in return a free subscription to one of the Danish *Acta* (see list in the *Quarterly Cumulative Index Medicus*), covering as many volumes as we receive.

Torkil Olsen
Exchange Librarian

BOOK REVIEWS

Diseases of the Tropics. By George C. Shattuck, M.D. 8°, cloth, 803 pp., with 131 illustrations and 26 tables. New York: Appleton-Century-Crofts, Incorporated, 1951. $10.00.

Modern war and travel have increased contact between the temperate and tropical regions to such an extent that a working knowledge of the prevalent tropical diseases has become necessary to the general practitioner. This book offers a concise but comprehensive account of the major tropical diseases likely to be encountered in practice in the temperate zone. Malaria, leishmaniasis, amebiasis, yaws, the typhus fevers, yellow fever, plague and cholera are stressed. Diseases of lesser importance have been more briefly but adequately described. Epidemiology, prophylaxis and control are outlined for each disease, making the book of great use to the public-health officer. Newer diagnostic technics are described in detail, as well as advances in treatments with sulfonamides and antibiotics where these seem promising.

About a quarter of the text is devoted to protozoan diseases, a quarter to bacterial diseases, an eighth to viral and rickettsial diseases, somewhat more to helminthic diseases and the rest to mycoses, nutritional disorders, noxious plants and animals and a discussion of climates and health. Short bibliographies of some of the more important references are appended to each chapter. The work is well indexed. The chapters on mycoses are the least satisfactory, as the author has evidently relied heavily on secondary sources and has had little personal experience with these diseases. The only lapsus calami detected occurs in this group; on page 617 the last sentence in the penultimate paragraph should read: "In the tissues, the North American type produces single buds, whereas the South American type exhibits multiple budding." As the mycoses described (except rhinosporidiosis) are as frequent in temperate climates as in the tropics and are better known from cases in temperate regions, these short chapters should not detract from the great merit of the work. The reviewer has found it very useful as a source book for his lectures in general bacteriology, as it brings together, in well digested form, much scattered literature that is not well covered in the usual elementary textbook.

Carroll S. Dodge, M.D.

Fifty Years of Medicine: A symposium from the British Medical Journal. 8°, cloth, 330 pp., with illustrations. London: British Medical Association, 1950. 15/.

In the issue of the *British Medical Journal* for January 7, 1950, there was a splendid survey of medicine and surgery as it has developed during the last fifty years. These articles were of such excellence that many considered them worthy of more permanent preservation in the form of a book. This book has now been published under the editorship of Dr. Hugh Clegg, with all the articles, by a team of distinguished investigators, now reprinted in clear type, along with the superb illustrations, many of them of great historical value. The editor has, for instance, had the title page of articles of outstanding merit photographed and in some cases has even taken advantage of the notes used by the investigator at the time an experiment was carried out. In addition, there are characteristic pictures of operations of fifty years ago, compared with those of today, and many others of equal value. The book is an outstanding record of the last fifty years of medicine, in which Great Britain has played such an important part.

Henry R. Viets, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Differential Diagnosis of Internal Diseases: Clinical analysis and synthesis of symptoms and signs. By Julius Bauer, M.D., clinical professor of medicine, College of Medical Evangelists, Los Angeles, senior attending physician, Los Angeles County General Hospital, consultant in medicine, White Memorial

Hospital, Long Beach Veterans Administration Hospital and Cedars of Lebanon Hospital, Los Angeles. 8°, cloth, 866 pp., with 56 illustrations. New York, Grune and Stratton, 1950. $12.00.

This new textbook is divided into two main parts on leading symptoms and leading signs. The part on leading signs discusses the general appearance (habits), hyperthermia, fever and infectious diseases, the diseases of the various systems of the body, (except the nervous system) and glycosuria. The material is well arranged and illustrated with case histories throughout the text. Lists of references are appended to the various chapters, and there are indexes of authors and subjects.

The Rhesus Danger: Its medical, moral and legal aspects. By R. N. C. McCurdy, M.B., Ch.B., D.P.H. 12°, paper, 138 pp. London: William Heinemann. Medical Books, Ltd., 1950. 5s net.

This monograph deals with the Rh problem in two parts. The first discusses the blood groups, the discovery of Rh, sensitization, treatment of hemolytic disease and racial distribution of blood groups. The second part is concerned with moral, social and legal aspects from the sexual point of view. The subjects covered in this part include contraception, sterilization, abortion, artificial insemination, divorce and population problems in relation to Rh. A summary of the pertinent literature is embodied throughout the text. There is a bibliography and an index.

Le salmonellosi nell'uomo. By G. Scotti and G. T. Sicca. With a preface by Prof. G. Monasterio. 8°, paper, 143 pp. Pisa: Omnia Medica, 1950. $3.50.

This monograph comprises a survey of the modern literature on salmonellosis in man. All phases of th disease are covered. There is a bibliography of eight pages.

Cancer Services and Facilities in the United States, 1950. By the Federal Security Agency, Public Health Service, National Cancer Institute of the National Institutes of Health. 8°, paper, 152 pp. Washington, D. C.: United States Government Printing Office, 1950. $0.35. PHS Publication No. 14.

This up-to-date report contains a summary for the nation at large and also for each individual state and territory. The pertinent information for each state concerning the current cancer situation is given in a tabular form. Previous reports of a like character were issued in 1946 and 1948.

Biological Antioxidants: Transactions of the fourth conference, December 8-9, 1949, New York, New York. Edited by Cosmo G. Mackenzie, Department of Biochemistry, University of Colorado School of Medicine. Associate editors: E. V. Jensen, departments of Surgery and Chemistry, University of Chicago School of Medicine, and Ralph T. Holman, Department of Biochemistry and Nutrition, Agricultural and Mechanical College of Texas. 8°, paper, 181 pp., with illustrations. New York: Josiah Macy, Jr., Foundation, 1950. $3.25.

This conference was attended by fourteen members and nine guests. Eight articles on the biochemistry of oxidation and on various antioxidants were read and discussed.

Blood Clotting and Allied Problems: Transaction of the third conference, January 23-24, 1950, New York, New York. Edited by Joseph E. Flynn, Department of Pathology, College of Physicians and Surgeons, Columbia University. 8°, cloth, 224 pp., with 52 illustrations and 32 tables. New York: Josiah Macy, Jr., Foundation, 1950. $3.00.

The conference was participated in by sixteen members and eight guests. Fifteen articles on the various anticoagulants and on blood clotting in general make up the text. The publishing is excellent and the book should be in all collections on the subject.

Wheeler and Jack's Handbook of Medicine. Revised by Robert Coope, M.D., B.Sc., F.R.C., physician, Liverpool Royal Infirmary, consulting physician, King Edward VII Sanatorium, Midhurst, physician, Liverpool Hospital for Diseases of the Chest and Liverpool and North-Western Chest Surgical Unit, visiting physician, Maghull Epileptic Homes, lecturer in clinical medicine, applied physiology and clinical chemistry, University of Liverpool, and examiner in medicine, Conjoint Board and University of Liverpool. Eleventh edition. 12°, cloth, 648 pp., with 62 illustrations. Baltimore: Williams and Wilkins Company, 1950. $5.00.

This British book was first published in 1894 and has gone through eighteen editions and reprintings prior to this new edition. The seventh edition was printed in 1937 and reprinted in 1940. The author has now entirely revised and in parts completely rewritten the text. The publishing is good; the printing was done in Great Britain. The manual reflects the present-day practice of medicine in England.

Your Prostate Gland: Letters from a surgeon to his father. By Reed M. Nesbit, M.D., professor of surgery, University of Michigan Medical School, and chief, section on urology, University Hospital, Ann Arbor, Michigan. With illustrations by Janet McLaughlin. 8°, cloth, 50 pp., with illustrations. Springfield, Illinois: Charles C Thomas, 1950. $2.00.

This book presents in simple form the information necessary for men afflicted with prostatic troubles. The author discusses briefly the anatomy of the prostate, its enlargement and the operations on the gland. The last chapter deals with cancer and the necessity of periodic examinations. The text is well written and the book should be in all medical collections for the laity.

Serum Sickness. By C. Frh. von Pirquet, M.D., and Bela Schick, M.D. Translated by Bela Schick, M.D. 8°, cloth, 130 pp., with 4 tables and 13 charts. Baltimore: The Williams and Wilkins Company, 1951. $3.50.

"Allergy" came into being with the publication of "Serumkrankheit" by von Pirquet and Schick in 1905. The original monograph was written in German, and Dr. Schick has now provided an English translation of this classical work. The book should be in all medical libraries and in the collections of all allergists.

Clinical Parasitology. By Charles F. Craig, M.D., M.A. (Hon.), Sc.D. (Hon.), D.S.M.; and Ernest C. Faust, M.A., Ph.D., William Vincent Professor of Tropical Diseases and Hygiene and head, Division of Parasitology, Department of Tropical Medicine and Public Health, Tulane University of Louisiana, New Orleans, consultant to the Surgeon General, United States Army, and consultant, United States Public Health Service. With a chapter on "Control of Medically Important Arthropods" by Albert Miller, B.S., M.S., Ph.D., associate professor of parasitology (medical entomology) in the Department of Tropical Medicine and Public Health, Tulane University of Louisiana. Fifth edition. 8°, cloth, 1032 pp., with 326 illustrations and 6 colored plates. Philadelphia: Lea and Febiger, 1951. $12.00.

This authoritative textbook has again been completely revised to bring the subject matter up to date. New chapters on epidemiology and insecticides and a textual synopsis of the arthropod-borne diseases of man have been added. There is an extensive bibliography and a good index; the publishing is excellent. The book is recommended for all collections on the subject.

Twentieth Anniversary Review of the Josiah Macy, Jr., Foundation. 8°, cloth, 110 pp., with 2 frontispieces. New York: Josiah Macy, Jr., Foundation, 1950. (Complimentary.)

This anniversary volume presents in brief the history of the work of the foundation, in its special fields of aging, psychosomatic medicine and medical education and practice. The small book should be in all collections on the history of medicine. It presents a summary of the excellent work carried on by the Macy Foundation.

Current Therapy 1951: Latest approved methods of treatment for the practicing physician. Edited by Howard F. Conn, M.D. 4°, cloth, 699 pp., with tables. Philadelphia: W. B. Saunders Company, 1951. $10.00.

This new volume is the joint work of a large number of contributors, all specialists in their particular subjects. The whole field of medicine is covered. Eighty-six of the

methods described have been developed since the publication of the 1950 volume. The volume should be valuable to the practicing physician.

The Amino Acid Composition of Proteins and Foods: Analytical methods and results. By Richard J. Block, Ph.D., associate, Department of Physiology and Biochemistry, New York Medical College, and research director, C. M. Armstrong, Incorporated; and Diana Bolling, B. S. Second edition. 8°, cloth, 576 pp., with illustrations, diagrams, tables and charts. Springfield, Illinois: Charles C Thomas, 1951. $10.50.

This standard reference book has been revised to bring it up to date, incorporating all the new developments made in the field since the publication of its first edition in 1945. There is an extensive bibliography. The book should be in all biochemical collections.

Psychosurgery: In the treatment of mental disorders and intractable pain. By Walter Freeman, M.D., Ph.D., professor of neurology, George Washington University, Washington, D.C., and James W. Watts, M.D., professor of neurological surgery, George Washington University. Second edition. 4°, cloth, 598 pp., with 156 illustrations and 21 tables. Springfield, Illinois: Charles C Thomas, 1950. $10.50.

This new edition of a standard book, first published in 1942, has been revised to bring the text up to date. The conclusions now drawn are based on a study of over 1000 cases. The original 80 cases reported in 1942 have been followed continuously, and many are now reported ten years or more after lobotomy. The text has been completely rewritten and reset in new type. The publishing is excellent. There is an extensive bibliography. The price is reasonable, and the book should be in all medical libraries and in the libraries of all brain surgeons.

A Textbook of the Practice of Medicine. By various authors. Edited by Frederick W. Price, M.D., F.R.S.Ed., C.M.Ed., F.R.C.P. Lond., M.D. Hon. Belf., consulting physician, Royal Northern Hospital and National Hospital for Diseases of the Heart, London. Eighth edition. 8°, cloth, 2076 pp., with 87 illustrations. New York: Oxford University Press, 1950. $9.00.

This composite textbook was first published in 1922. Its soundness and popularity is attested to by the large number of its editions and reimpressions, — twenty-one to date. The text is the joint work of thirty eminent English physicians. The whole field of medicine is covered, including psychologic medicine. There is an elaborate, comprehensive index, and the publishing is excellent. The price is reasonable. The book, depicting current English medical practice, should be in all medical libraries.

Memorias do Instituto Oswaldo Cruz, Rio de Janeiro, Brazil. Comemorativo do cinqüentenário do Instituto Oswaldo Cruz. Vol. 48. 4°, paper, 732 pp., with illustrations. Rio de Janeiro: Servico Gráfico do Instituto Brasileiro de Geografia e Estatística, 1950.

This serial volume contains thirty-seven articles on leprosy, typhus, parasites and parasitic diseases and other tropical conditions. The text proper is preceded by a historical sketch of the institute, comprising fifty pages, twenty-four full-page illustrations and one plan, written in honor of its fiftieth anniversary. The publishing is excellent, and the series should be in all collections on tropical medicine.

NOTICES

ANNOUNCEMENT

Dr. Schoul Levison announces the opening of an office at 117 Bay State Road, Boston, for the practice of neurology and psychiatry.

AMERICAN FEDERATION FOR CLINICAL RESEARCH: BOSTON CHAPTER

The Boston Chapter of the American Federation for Clinical Research will hold a meeting on November 13, at 8:00 p.m., at the Evans Memorial Hospital. The program is as follows:

Some Effects of Carbonic-Anhydrase Inhibitor on Renal Function. Dr. Arnold S. Relman, Dr. William Hodges, Dr. Lamont E. Danzig, Dr. Joseph Greaney and Dr. William B. Schwartz (Massachusetts Memorial Hospital and the New England Center Hospital).

Observations on Pulmonary Infarction Following Cardiac Catheterization. Dr. Hector E. J. Houssay, Dr. Florence W. Haynes and Dr. Lewis Dexter (Peter Bent Brigham Hospital).

Observations on the Role of "Selective Sequestration" of Platelets by the Spleen in Idiopathic Thrombocytopenic Purpura. Dr. Mario Stefanini, Dr. Jyoti B. Chatterjea and Dr. William Dameshek (New England Center Hospital).

Antigenic Properties of Human Leukocytes. Dr. W. C. Maloney, Dr. M. Saint Paul and Dr. J. Mc A'Nulty (Rh Laboratory of the Boston City Hospital).

Dynamics and Clinical Picture of Patients with Mitral Regurgitation and Stenosis. Dr. Richard Gorlin and Dr. Benjamin Lewis (Peter Bent Brigham Hospital).

COUNCIL OF NEW ENGLAND STATE MEDICAL SOCIETIES

A Symposium on Professional Relations in Medical-Care Insurance will be presented by the Council of New England State Medical Societies at the Copley Plaza Hotel, Boston, on Sunday, November 18, at 2:00 p.m. Dr. Joseph H. Howard, of Bridgeport, Connecticut, will preside.

PROGRAM

2:00 p.m. Call to order and outline of purposes of the conference. Dr. Joseph H. Howard.

Symposium on Professional Relations in Medical-Care Insurance. Dr. J. Danaher, Torrington, Connecticut, chairman, Professional Policy Committee of the Connecticut Medical Service, Moderator.

National Trends in Blue Shield Developments. Frank E. Smith, Ph.D., Director of National Association of Blue Shield Plans, Chicago, Illinois.

The Relation of Physicians to Blue Shield. Dr. Charles G. Hayden, Executive Director, Massachusetts Blue Shield, Boston.

Professional Relations in Medical-Service Insurance Carried by Commercial Insurance Companies. Speaker to be announced.

Medical-Service Insurance Plan Viewed by Practicing Physicians. Dr. Charles L. Farrell, Pawtucket, Rhode Island; Dr. Joseph A. Holmes, Waltham, Massachusetts; and Dr. Daniel G. Sullivan, Nashua, New Hampshire.

Fee-Table Construction and Philosophy. Dr. William Horton, managing director, Connecticut Medical Service, New Haven, Connecticut.

General Discussion

6:00 p.m. Social hour and cocktails.

6:45 p.m. Dinner.

After-dinner speaker: Dr. Louis H. Bauer, Hampstead, New York, president-elect, American Medical Association.

All members of the State Medical Societies in New England and the Woman's Auxiliaries are invited to attend.

NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS

A meeting of the New England Society of Anesthesiologists will be held in the Auditorium, Building A, Boston University School of Medicine, on Tuesday, November 13, at 7:30 p.m.

The program is as follows:

Air Embolism Associated with Intravenous Therapy. Case report: Dr. Edmund F. Neves; discussion: Dr. Herbert Ebner.

A Compatible Dextrose-Saline and Blood Solution. Dr. Donald Buschle.

Two New Oxygen Masks. Dr. Arnold S. Gale.

Intermittent Positive Pressure Breathing. Dr. Meyer Saklad.

HARVARD MEDICAL SOCIETY

The Harvard Medical Society will hold a meeting on Tuesday evening, November 13, in Amphitheatre D of the Harvard Medical School, at 8:00 p.m. The program will be presented by the Boston Lying-in Hospital, with Dr. Duncan E. Reid presiding.

PROGRAM

Observations on the Uteroplacental Circulation. Dr. Seymour L. Romney and Dr. Duncan E. Reid.
Circulating Red-Cell Volume in Normal Pregnancy. Dr. William L. Caton, Dr. Charles C. Roby, Dr. Duncan E. Reid and Dr. John G. Gibson, II.
In-Vitro Studies on the Metabolism of the Placenta. Dr. Claude A. Villee, Jr.
Afibrinogenemic States in Pregnancy. Dr. Alfred E. Weiner, Dr. Charles C. Roby and Dr. Duncan E. Reid.
Antitoxic Action of Penicillin Unassociated with Its Antibiotic Properties. Dr. Olive W. Smith and Dr. George Van S. Smith.

NORFOLK DISTRICT MEDICAL SOCIETY

The following programs will be held by the Norfolk District Medical Society at the Boston Medical Library, 8 Fenway, Boston, at 8:00 p.m. (except as noted).

Tuesday, November 27 (Meeting to be held at Joslin Auditorium, New England Deaconess Hospital). "Headache." Dr. John R. Graham and associates.
Tuesday, January 22 (Meeting to be held at West Roxbury Veterans Administration Hospital). West Roxbury Veterans Administration Hospital Staff Round Table (subject to be announced).
Tuesday, February 26. "Non-Endocrine Endocrinology." Dr. Edwin B. Astwood and associates.
Tuesday, March 25. "Ovarian Dysfunction" (For the General Practitioner). Dr. Joe V. Meigs and associates.
Tuesday, April 22. Annual meeting.
Wednesday, May 7 (Place to be announced). Annual dinner.

NEW YORK STATE SOCIETY OF ANESTHESIOLOGISTS

The New York State Society of Anesthesiologists will hold its Fifth Annual Postgraduate Assembly December 5-8 at the Hotel New Yorker, New York City. The program will include ten scientific sessions in panel form. One panel will be presented by residents and fellows in anesthesiology, who will discuss original investigations in which they have participated. Physicians desiring to attend may secure a registration form from the office of the society at 137 West 11th Street, New York City.

LIFE INSURANCE MEDICAL RESEARCH FUND GRANTS AND FELLOWSHIPS

Applications for grants in aid of research on cardiovascular problems for 1952 will be received by the Life Insurance Medical Fund up to November 15, 1951. Support is available for physiologic, biochemical and other basic research relating to cardiovascular problems, as well as for clinical investigation in this field. Preference is given to fundamental research. It is expected that these grants will total about $600,000.

Applications for postdoctoral fellowships for training in research in 1952–1953 may be made until November 1, 1951. Preference will be given to candidates who wish to work in the general field of cardiovascular function or disease and to candidates who wish to work in institutions other than those in which they have obtained most of their experience. A doctor's degree (M.D. or Ph.D.) or its equivalent is required. The annual stipend varies, being as a rule between $3000 and $4000; larger amounts are granted in special cases. Approximately 15 new postdoctoral fellowships will be available.

New grants and fellowships will become available on July 1, 1952.

A number of predoctoral fellowships for basic training in research will also be awarded. Details are available on request.

Further information and application blanks may be secured from the Scientific Director, Life Insurance Medical Research Fund, 2 East 103d Street, New York 29, New York.

AMERICAN CANCER SOCIETY GRANTS FOR CANCER RESEARCH

Announcement is made of grants for American Cancer Society Scholars in Cancer Research. A limited number of American Cancer Society Scholars are appointed annually on recommendation of the Committee on Growth of the National Research Council. A grant of $18,000, payable over three years, will be made directly to each scholar's institution by the American Cancer Society as a contribution toward his support or his research or both.

Medical schools, hospitals, research institutes and other institutions with a primary or substantial interest in cancer research are invited to submit applications for these grants. Applications for grants to be effective July 1, 1952, should be submitted prior to January 1, 1952. Inquiries or requests for application forms should be addressed to the Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D. C.

Inquiries concerning Damon Runyon Clinical Fellowships, formerly recommended by the Committee on Growth, should now be addressed to the Damon Runyon Memorial Fund, Hotel Astor, Broadway and 44th Street, New York 19, New York.

SOCIETY MEETINGS AND CONFERENCES

NOVEMBER 2 AND 3. Eastern Section, American Trudeau Society. Page 350, issue of August 30.

NOVEMBER 3–28. The Springfield Hospital. Page 670, issue of October 25.

NOVEMBER 4 AND 5. American Society for the Study of Arteriosclerosis. Page xv, issue of July 12.

NOVEMBER 5. Beth Israel Hospital House Officers' Colloquium. Page 590, issue of October 11.

NOVEMBER 5–9. American College of Surgeons. Page 388, issue of September 6.

NOVEMBER 5, 19 AND 26. Beth Israel Hospital House Officers' Colloquium. Page 590, issue of October 11.

NOVEMBER 6. Edward K. Dunham Lecture. Page 669, issue of October 25.

NOVEMBER 6. The New England Diabetes Association. Page 669, issue of October 25.

NOVEMBER 6, 8, 20 AND 27. Boston City Hospital House Officers' Association. Page 669, issue of October 25.

NOVEMBER 7. Salmon Memorial Lecture. Page 548, issue of October 4.

NOVEMBER 7–9. New England Postgraduate Assembly. Hotel Statler, Boston. Program, page xiii, issue of October 11.

NOVEMBER 7–19. Pan-Pacific Surgical Association. Page 820, issue of May 24.

NOVEMBER 8. The New England Rheumatism Association. Page 669, issue of October 25.

NOVEMBER 8. New England Cardiovascular Society. Page 669, issue of October 25.

NOVEMBER 8. Diverticulitis — Conservative or Radical Management. Dr. Joseph Tartakoff. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

NOVEMBER 9. Rocky Mountain Harvard Medical School Alumni Association. Page 548, issue of October 4.

NOVEMBER 9, 16, 23 AND 30, DECEMBER 7, 14, 21 AND 28 AND JANUARY 4. New England Deaconess Hospital Clinics. Page 548, issue of October 4.

NOVEMBER 13. Harvard Medical Society. Notice above.

NOVEMBER 13. American Federation for Clinical Research (Boston Chapter). Page 709.

NOVEMBER 13. New England Society of Anesthesiologists. Page 709.

NOVEMBER 13. Springfield Academy of Medicine. Page 548, issue of October 4.

NOVEMBER 14. Salmon Memorial Lecture. Page 548, issue of October 4.

NOVEMBER 14. Northeastern New York Radiological Society. University Club, Albany, New York.

NOVEMBER 14 AND 15. Diabetes Fair. New England Diabetes Association. Page 669, issue of October 25.

NOVEMBER 18. Council of New England State Medical Societies. Page 709.

NOVEMBER 20. Salmon Memorial Lecture. Page 548, issue of October 4.

NOVEMBER 21. Alpha Omega Alpha Lecture. Page 669, issue of October 25.

NOVEMBER 27, JANUARY 22, FEBRUARY 26, MARCH 25 AND APRIL 22. Norfolk District Medical Society. Notice above.

DECEMBER 2. American Academy of Dental Medicine. Page 548, issue of October 4.

DECEMBER 5–8. New York State Society of Anesthesiologists. Notice above.

DECEMBER 11–19. International Congress on Mental Health. Page xiii, issue of July 26.

(Notices concluded on page xi)